

## 11INVENTOR SEARCH

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FILE CONTENT:1840 - 1 Apr 2007 VOL 146 ISS 15

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\*\*\*\*\*

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This file contains CAS Registry Numbers for easy and accurate substance identification.

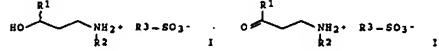
L2 12 SEA FILE=CASREACT ABB=ON MICHEL D7/AU  
L3 72 SEA FILE=CASREACT ABB=ON 3-AMINO ALCOHOL  
L4 2 SEA FILE=CASREACT ABB=ON L2 AND L3

> d iell 14 1

L4 ANSWER 1 OF 2 CASREACT COPYRIGHT 2007 ACS ON STN  
ACCESSION NUMBER: 145:271387 CASREACT Full-text  
TITLE: Process for the preparation of enantiomerically pure 1-substituted-3-amino alcohols using methyl ketones, primary amines, formaldehydes and sulfonic acids  
INVENTOR(S): Brieden, Walter; Clausen, Martin; McGarity, John; Mettler, Hanspeter; Michel, Dominique  
PATENT ASSIGNEE(S): Lonza A.-G., Switz.  
SOURCE: PCT Int. Appl., 38pp.  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
CLASSIFICATION: 23-15 (Aliphatic Compounds)  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006087166	A1	20060824	WO 2006-EP1334	20060214
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,			

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KB, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LV, LY, MA, MD, MG, MK, MN, MM, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TO, BM, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, ZW  
EP 1693371 A1 20060823 EP 2005-3657 20050221  
R: AT, BS, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU  
PRIORITY APPLN. INFO.: EP 2005-3657 20050221  
OTHER SOURCE(S): MARPAT 145:271387  
GRAPHIC IMAGE:



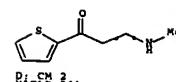
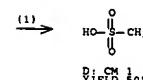
## ABSTRACT:

Provided is a process for the preparation of N-monosubstituted  $\beta$ -aminoalcoholsulfonates of formula I. Compds. of formula I wherein R1 is (un)substituted C6-20 aryl or (un)substituted C4-12 heteroaryl; R2 is Cl-4-alkyl or (un)substituted C6-20 aryl; R3 is selected from the group consisting of Cl-8 alkyl, C6-20 cycloalkyl, C6-20 aryl and C7-20 aralkyl residues, and the process for preparing compds. of formula I are claimed. The process comprising the steps of a) reacting a Me ketone, a primary amine, formaldehyde and a sulfonic acid, at a pressure above 1.5 bar, optionally in a organic solvent, said organic solvent optionally containing water, to afford N-monosubstituted  $\beta$ -amino ketone sulfonates of formula II, wherein R1, R2 and R3 are as defined above, and b) asym. hydrogenating said sulfonates in the presence of a base and a catalyst, comprising a transition metal and a diphosphine ligand, in a polar solvent, optionally in the presence of water.

SUPPL. TERM: amino alc sulfonate asym prep; methyl ketone amine formaldehyde sulfonic acid  
INDEX TERM: Ketones, preparation  
ROLE: SPN (Synthetic preparation); PREP (Preparation)  
(amine; preparation of enantiomerically pure sulfonate salts of substituted amino alics. and amino ketones by reacting Me ketones, primary amine, formaldehyde and sulfonic acids)  
INDEX TERM: Alcohols, preparation  
ROLE: SPN (Synthetic preparation); PREP (Preparation)  
(chiral, amino; preparation of enantiomerically pure sulfonate salts of substituted amino alics. and amino ketones by reacting Me ketones, primary amine, formaldehyde and sulfonic acids)  
INDEX TERM: Amines, preparation  
ROLE: SPN (Synthetic preparation); PREP (Preparation)

(keto; preparation of enantiomerically pure sulfonate salts of substituted amino alics. and amino ketones by reacting Me ketones, primary amine, formaldehyde and sulfonic acids)  
INDEX TERM: Asymmetric synthesis and induction  
(Preparation of enantiomerically pure sulfonate salts of substituted amino alics. and amino ketones by reacting Me ketones, primary amine, formaldehyde and sulfonic acids)  
INDEX TERM: Hydrogenation  
Hydrogenation catalysts  
(stereoselective; preparation of enantiomerically pure sulfonate salts of substituted amino alics. and amino ketones by reacting Me ketones, primary amine, formaldehyde and sulfonic acids)  
INDEX TERM: 752258-19-8, (R,R,S,S)-TangPhos  
ROLE: CAT (Catalyst use); USES (Uses)  
(R,R,S,S)-TangPhos, catalyst; preparation of enantiomerically pure sulfonate salts of substituted amino alics. and amino ketones by reacting Me ketones, primary amine, formaldehyde and sulfonic acids)

RX(1) OF 6 A + B + C ==> D



RX(1) RCT A 206872-28-8, B 88-15-3, C 50-00-0

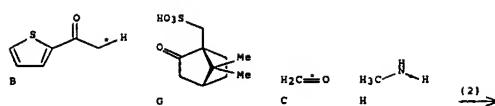
STAGE(1)  
SOL 64-17-5 EtOH  
CON 3 hours, 120 deg C, 4.5 bar

STAGE(2)  
SOL 64-17-5 EtOH, 141-78-6 AcOEt  
CON 30 minutes, 25 deg C

PRO D 906812-48-4

NTB paraformaldehyde used, autoclave used, analogs prepd. similarly, thermal

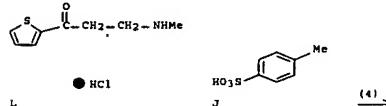
RX(2) OF 6 B + G + C + H ==&gt; I



RX(3) RCT B 88-15-3, J 104-15-4, C 50-00-0, H 74-89-5

STAGE(1)  
SOL 64-17-5 EtOH  
CON 4 hours, 120 deg CSTAGE(2)  
SOL 64-17-5 EtOH, 141-78-6 AcOEt  
CON 30 minutes, 25 deg CPRO K 863094-23-9  
NTE paraformaldehyde used, autoclave used, thermal

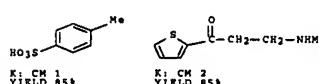
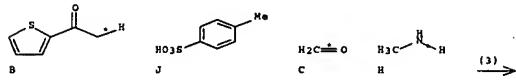
RX(4) OF 6 L + J ==&gt; K



RX(2) RCT B 88-15-3, G 3144-16-9, C 50-00-0, H 74-89-5

STAGE(1)  
SOL 64-17-5 EtOH  
CON 4 hours, 120 deg C, 4.5 - 4.8 barSTAGE(2)  
SOL 64-17-5 EtOH, 141-78-6 AcOEt  
CON 30 minutes, 25 deg CPRO I 906812-50-8  
NTE paraformaldehyde used, autoclave used, thermal

RX(3) OF 6 B + J + C + H ==&gt; K



RX(4) RCT L 645411-16-1

STAGE(1)  
RGT M 1310-73-2 NaOH  
SOL 7732-18-5 Water, 1634-04-4 t-BuOMe  
CON SUBSTAGE(1) 15 minutes, 5 deg C  
SUBSTAGE(2) 10 minutes, 5 deg CSTAGE(2)  
RCT J 104-15-4  
SOL 67-56-1 MeOH  
CON SUBSTAGE(1) 15 minutes, 5 deg C

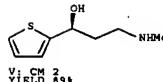
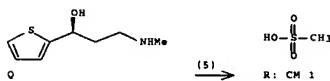
5

6

SUBSTAGE(2) 30 minutes, 25 deg C

PRO K-863094-23-9  
NTE analogs prep. similarly

RX(5) OF 6 Q ==&gt; R



RX(6) RCT Q 116539-55-0, G 3144-16-9

STAGE(1)  
SOL 64-17-5 EtOH, 141-78-6 AcOEt  
CON SUBSTAGE(1) 40 minutes, 30 deg C  
SUBSTAGE(2) 15 minutes, 50 deg CSTAGE(2)  
SOL 141-78-6 AcOEt  
CON SUBSTAGE(1) 15 minutes, reflux  
SUBSTAGE(2) 30 minutes, reflux -> 25 deg C

PRO V 906812-57-5

&gt; d i all 14 2

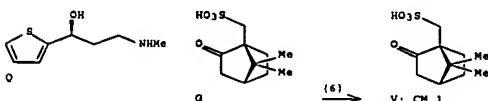
L4 ANSWER 2 of 2 CASREACT COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 143:248273 CASREACT Full-text  
 TITLE: Preparation of enantiomerically pure 1-substituted-3-amino alcohols  
 INVENTOR(S): Michel, Dominique  
 PATENT ASSIGNEE(S): Lonza A.-G., Switz.  
 SOURCE: Eur. Pat. Appl., 14 pp.  
 CODEN: SPXXDN  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 INT. PATENT CLASSIFI.:  
 MAIN: C07D333-20  
 SECONDARY: C07D333-22; C07C213-00; C07B05J-00  
 CLASSIFICATION: 27-8 (Heterocyclic Compounds (One Hetero Atom))  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1566383	A1	20050824	EP 2004-3809	20040219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, PL, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2005215906	A1	20050901	AU 2005-215906	20050221
CA 2556691	A1	20050901	CA 2005-2556691	20050221
WO 2005080370	A1	20050901	WO 2005-EP1781	20050221
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, GE, GH, GM, HR, ID, IL, IS, JP, KS, KO, KP, KR, KZ, LC, LK, LR, LS, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				

RX(5) RCT Q 116539-55-0

STAGE(1)  
RCT S 584-08-7 K2CO3  
CAT 528814-26-8 1,1'-Bi-1H-isophosphindole,  
2,2'-bis(1,1-dimethylethyl)-2',3',3'-tetrahydro-  
(1R,1'S,2'S,2'S)-  
SOL 7732-18-5 Water, 67-56-1 MeOH  
CON room temperatureSTAGE(2)  
RCT T 1333-74-0 H2  
CON 21 hours, 40 deg C, 10 barPRO R 906812-56-4  
NTE analogs prep. similarly, autoclave used, high pressure,  
stereoselective

RX(6) OF 6 Q + G ==&gt; V



RW: BW, GH, GM, KR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM.  
 AZ, BY, KG, KZ, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, TR, BP, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG  
 EP 1720852 A1 20061115 EP 2005-715425 20050221  
 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BP, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, NE, SN, TD, TG  
 CN 1923169 A 20070228 CN 2005-80005452 20050221  
 NO 200604017 A 20060915 NO 2006-4017 20060906  
 PRIORITY APPLN. INFO.: EP 2004-3809 20040219  
 EP 2004-10043 20040428  
 WO 2005-EP1781 20050221

OTHER SOURCE(S): MARPAT 143:248273

## ABSTRACT:

Provided is a process for the preparation of enantiomerically pure 1-substituted 3-amino alcs. (R)- or (S)-RO-CH<sub>2</sub>CH<sub>2</sub>NR<sub>2</sub> (R<sub>1</sub> = 2-thienyl, 2-furyl, Ph, substituted 2-chienyl, substituted 2-furyl, substituted Ph; R<sub>2</sub> = Cl-C<sub>4</sub>-alkyl, Ph, substituted Cl-C<sub>4</sub>-alkyl, substituted Ph), particularly (S)-(-)- and (R)-(-)-3-N-methylamino-1-(2-thienyl)-1-propanol, by asym. hydrogenating salts of RICOCH<sub>2</sub>CH<sub>2</sub>NR<sub>2</sub> using Rh and an asym. ligand.

SUPPL. TERM: alc amino asym prep rhodium chiral ligand hydrogenation; hydrogenation asym amino ketone amino alc prep

INDEX TERM: Alcohols, preparation  
 ROLE: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)  
 (amino; asym. synthesis of 1-substituted 3-amino alcs. via hydrogenation of amino ketones)

INDEX TERM: Ketones, reactions  
 ROLE: RCT (Reactant); RACT (Reactant or reagent)  
 (amino; asym. synthesis of 1-substituted 3-amino alcs. via hydrogenation of amino ketones)

INDEX TERM: Asymmetric synthesis and induction  
 (asym. synthesis of 1-substituted 3-amino alcs. via hydrogenation of amino ketones)

INDEX TERM: Amines, reactions  
 ROLE: RCT (Reactant); RACT (Reactant or reagent)  
 (ket; asym. synthesis of 1-substituted 3-amino alcs. via hydrogenation of amino ketones)

INDEX TERM: Hydrogenation  
 (stereoselective; asym. synthesis of 1-substituted 3-amino alcs. via hydrogenation of amino ketones)

INDEX TERM: 116539-55-0P, (S)-(-)-3-(N-Methylamino)-1-(2-thienyl)-1-propanol 116539-57-2P 863094-39-7P 863094-46-6P  
 ROLE: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)  
 (asym. synthesis of 1-substituted 3-amino alcs. via hydrogenation of amino ketones)

INDEX TERM: 569687-76-9P 645411-16-1P, 3-(N-Methylamino)-1-(2-thienyl)-1-propanone hydrochloride 863094-06-8P 863094-15-9P  
 863094-23-9P 863094-31-9P  
 ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (asym. synthesis of 1-substituted 3-amino alcs. via hydrogenation of amino ketones)

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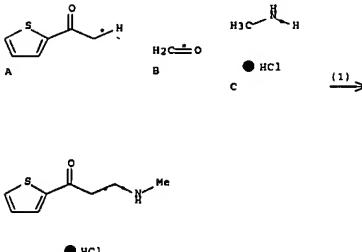
INDEX TERM: 1133545-16-1 133545-17-2 136735-95-0 248244-33-9  
 486429-94-1 752258-19-8  
 ROLE: RGT (Reagent); RACT (Reactant or reagent)  
 (asym. synthesis of 1-substituted 3-amino alcs. via hydrogenation of amino ketones)

INDEX TERM: 116539-56-1P 863094-12-6P 863094-19-3P 863094-27-3P  
 863094-35-3P  
 ROLE: SPN (Synthetic preparation); PREP (Preparation)  
 (asym. synthesis of 1-substituted 3-amino alcs. via hydrogenation of amino ketones)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):  
 (1) Becker, H; WISSENSCHAFTLICHE ZEITSCHRIFT DER TECHNISCHEN HOCHSCHULE FÜR CHEMIE 1969, V11(1), P38  
 (2) Fujisawa Pharm Co Ltd; JP 05070412 A 1993 CAPLUS  
 (3) Jia, A; WO 03070720 A 2003 CAPLUS  
 (4) Lilly Co B11; EP 0457559 A 1991 CAPLUS  
 (5) Lonza Ag; WO 2004005239 A 2004 CAPLUS  
 (6) Lonza Ag; WO 2004005307 A 2004 CAPLUS  
 (7) Michael, R; US 6008412 A 1999 CAPLUS  
 (8) Robertson, D; JOURNAL OF MEDICINAL CHEMISTRY 1988, P1412 CAPLUS  
 (9) Sakai, K; TETRAHEDRON: ASYMMETRY 2003, V14(12), P1631 CAPLUS  
 (10) Sakuraba, S; CHEMICAL AND PHARMACEUTICAL BULLETIN 1995, V43(5), P748 CAPLUS

RX(1) OF 31 A + B + C ==&gt; D...

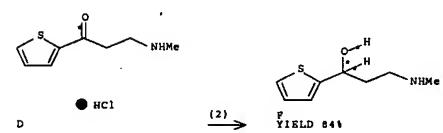


D YIELD 71%

RX(1) RCT A 88-15-3, B 50-00-0, C 593-51-1  
 PRO D 645411-16-1  
 SOL 64-17-5 EtOH  
 CON SUBSTAGE(1) 9 hours, 120 - 130 deg C  
 SUBSTAGE(2) 130 deg C -> 20 deg C  
 NTE paraformaldehyde used, autoclave used

10

RX(2) OF 31 ...D ==&gt; F



RX(2) RCT D 645411-16-1

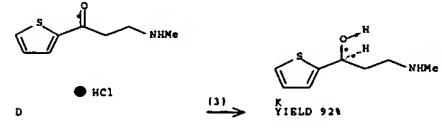
STAGE(1)  
 RGT G 1310-73-2 NaOH  
 SOL 7732-18-5 Water, 64-17-5 EtOH  
 CON 5 minutes, 4 deg C

STAGE(2)  
 RGT H 16940-66-2 NaBH4  
 CON SUBSTAGE(1) 30 minutes, 4 deg C  
 SUBSTAGE(2) 4 hours, 4 deg C

STAGE(3)  
 RGT I 67-64-1 Me2CO  
 CON SUBSTAGE(1) 5 minutes  
 SUBSTAGE(2) 10 minutes

PRO F 116539-56-1  
 NTE incremental addition of sodium borohydride in second stage

RX(3) OF 31 ...D ==&gt; K



RX(3) RCT D 645411-16-1

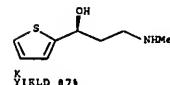
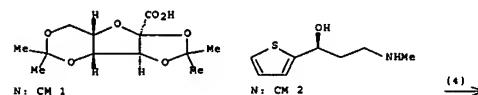
STAGE(1)  
 RGT G 1310-73-2 NaOH  
 SOL 67-56-1 MeOH  
 CON room temperature

STAGE(2)  
 SOL 67-56-1 MeOH  
 CON SUBSTAGE(1) room temperature  
 SUBSTAGE(2) room temperature -> 50 deg C

STAGE(3)  
 RGT L 1333-74-0 H2  
 CON SUBSTAGE(1) 50 deg C, 30 bar  
 SUBSTAGE(2) 5 hours, 50 deg C  
 SUBSTAGE(3) 50 deg C -> room temperature

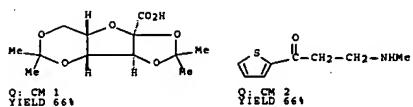
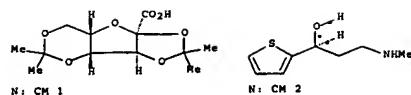
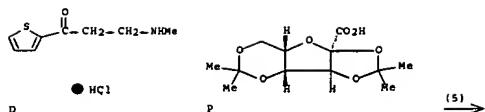
PRO K 116539-55-0  
 NTE [Rn(S,S)-Me-Duphos]BF4 used as catalyst stage 2, stereoselective, autoclave used, high pressure in last stage, ee = 97%, optimized on catalyst

RX(4) OF 31 ...N ==&gt; K



PRO F 116539-55-0  
 RGT G 1310-73-2 NaOH  
 PRO K 116539-55-0  
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2  
 CON SUBSTAGE(1) room temperature  
 SUBSTAGE(2) 15 minutes, room temperature  
 NTE incremental addition of reactant

RX(5) OF 31 ...D + P ==&gt; Q...

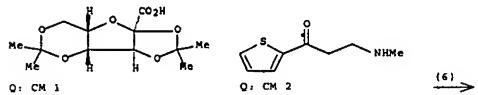


RX(5) RCT D 645411-16-1

STAGE(1)  
RCT Q 1310-73-2 NaOH  
SOL 7732-18-5 Water, 1634-04-4 t-BuOMe  
CON SUBSTAGE(1) room temperature  $\rightarrow$  0 deg C  
SUBSTAGE(2) 15 minutes, 0 deg C  
SUBSTAGE(3) 10 minutes, 0 deg C

STAGE(2)  
RCT P 18467-77-1  
SOL 1634-04-4 t-BuOMe  
CON room temperature

PRO Q 863094-06-8  
NTE scalable

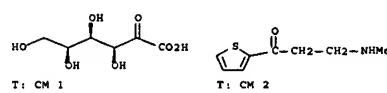
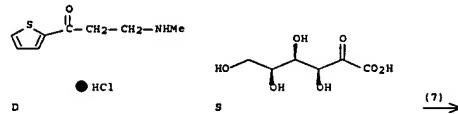
RX(6) OF 31 ...Q  $\rightarrow$  N...

RX(6) RCT Q 863094-06-8

STAGE(1)  
SOL 67-56-1 MeOH  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) room temperature  
SUBSTAGE(3) room temperature  $\rightarrow$  50 deg C

STAGE(2)  
RGT L 1333-74-0 H2  
CON SUBSTAGE(1) 50 deg C, 30 bar  
SUBSTAGE(2) 5 hours, 50 deg C  
SUBSTAGE(3) 50 deg C  $\rightarrow$  room temperature

PRO N 569687-76-9  
NTE (R(R,S,S)-tangphos)BF4 used as catalyst  
stage 1, stereoselective, high pressure in last stage, autoclave used, ee = 95%, conversion is 100%

RX(7) OF 31 ...D + S  $\rightarrow$  T

RX(7) RCT D 645411-16-1

STAGE(1)  
RCT G 1310-73-2 NaOH

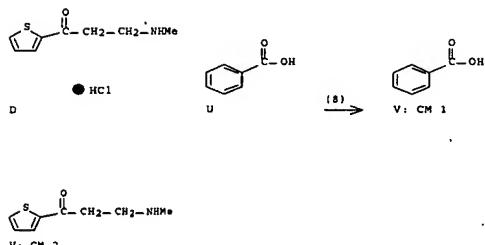
13

14

SOL 7732-18-5 Water, 1634-04-4 t-BuOMe  
CON SUBSTAGE(1) room temperature  $\rightarrow$  10 deg C  
SUBSTAGE(2) 5 - 10 deg C  
SUBSTAGE(3) 15 minutes, 5 - 10 deg C

STAGE(2)  
RCT S 526-98-7  
SOL 1634-04-4 t-BuOMe  
CON 15 minutes, <10 deg C

PRO T 863094-12-6

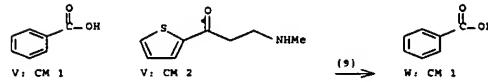
RX(8) OF 31 ...D + U  $\rightarrow$  V...

RX(8) RCT D 645411-16-1

STAGE(1)  
RCT Q 1310-73-2 NaOH  
SOL 7732-18-5 Water, 1634-04-4 t-BuOMe  
CON SUBSTAGE(1) room temperature  $\rightarrow$  10 deg C  
SUBSTAGE(2) 5 - 10 deg C  
SUBSTAGE(3) 15 minutes, 5 - 10 deg C

STAGE(2)  
RCT U 65-85-0  
SOL 1634-04-4 t-BuOMe  
CON 15 minutes, <10 deg C

PRO V 863094-15-9

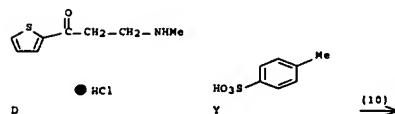
RX(9) OF 31 ...V  $\rightarrow$  W

RX(9) RCT V 863094-15-9

STAGE(1)  
CAT 205064-10-4 Rhodium(I)-, [(1,2,5,6- $\eta$ )-1,5-cyclooctadiene][(2S,2'S,5S,5'S)-1,1'-((1,2-phenylene)bis(2,5-dimethylphospholane- $\kappa$ P))]-, tetrafluoroborate(1-)  
SOL 67-56-1 MeOH  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) room temperature  $\rightarrow$  50 deg C

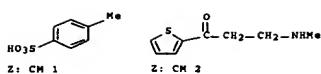
STAGE(2)  
RGT L 1333-74-0 H2  
CON SUBSTAGE(1) 50 deg C, 30 bar  
SUBSTAGE(2) 5 hours, 50 deg C  
SUBSTAGE(3) 50 deg C  $\rightarrow$  room temperature

PRO W 863094-19-3  
NTE stereoselective, high pressure in last stage, autoclave used, ee = 96.7%, conversion is 99%

RX(10) OF 31 ...D + Y  $\rightarrow$  Z...

15

16



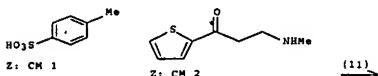
RX(10) RCT D 645411-16-1

STAGE(1)  
RCT G 1310-73-2 NaOH  
SOL 7732-18-5 Water, 1634-04-4 t-BuOMe  
CON SUBSTAGE(1) room temperature -> 10 deg C  
SUBSTAGE(2) 5 - 10 deg C  
SUBSTAGE(3) 15 minutes, 5 - 10 deg C

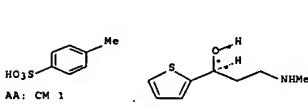
STAGE(2)  
RCT Y 104-15-4  
SOL 1634-04-4 t-BuOMe  
CON 15 minutes, <10 deg C

PRO Z 863094-23-9

RX(11) OF 31 ...Z ==&gt; AA



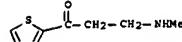
(11)



RX(11) RCT Z 863094-23-9

STAGE(1)  
CAT 205064-10-4 Rhodium(1+), [(1,2,5,6- $\eta$ )-1,5-cyclooctadiene][(2S,2'S,5S,5'S)-1,1'-(1,2-phenylene)bis[2,5-dimethylphospholane- $\kappa$ P]]-, tetrafluoroborate(1-)  
SOL 67-56-1 MeOH  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) room temperature -> 50 deg C

RX(12) OF 31 ...D + AB ==&gt; AC...



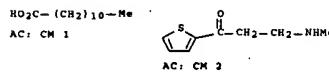
● HCl

D

HO<sub>2</sub>C-(CH<sub>2</sub>)<sub>10</sub>-Me

AB

(12) →



RX(12) RCT D 645411-16-1

STAGE(1)  
RCT G 1310-73-2 NaOH  
SOL 7732-18-5 Water, 1634-04-4 t-BuOMe  
CON SUBSTAGE(1) room temperature -> 10 deg C  
SUBSTAGE(2) 5 - 10 deg C  
SUBSTAGE(3) 15 minutes, 5 - 10 deg C

STAGE(2)  
RCT AB 143-07-7  
SOL 1634-04-4 t-BuOMe  
CON SUBSTAGE(1) 15 minutes, <10 deg C  
SUBSTAGE(2) 1 hour

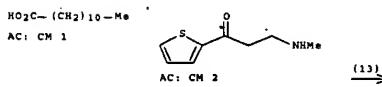
PRO AC 863094-31-9

RX(13) OF 31 ...AC ==&gt; AD

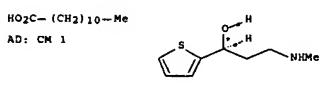
PRO AC 863094-31-9

17

18



(11)



REACTION SEARCH

10/520362

FILE 'CASREACT' ENTERED AT 15:29:11 ON 03 APR 2007  
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FILE CONTENT: 1840 - 1 Apr 2007 VOL 146 ISS 15

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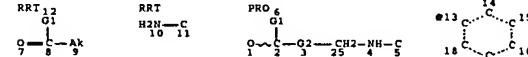
\*\*\*\*\*  
\* CASREACT now has more than 12 million reactions \*  
\*\*\*\*\*

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999) provided by Infochem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L15 STR

Ak@19 Ak-D-Ak Ak-Y  
#20 21 22 #23 24

VAR G1=19/20/23/13

RSP G2=(0-2) CH2

NODE ATTRIBUTES:

NSPEC IS RC AT 5

NSPEC IS RC AT 11

CONNECT IS EI RC AT 1

CONNECT IS EI RC AT 9

CONNECT IS EI RC AT 19

CONNECT IS EI RC AT 22

DEFAULT MLEVEL IS ATOM

GOCAT IS LOC SAT AT 9

DEFAULT ECLEVEL IS LIMITED

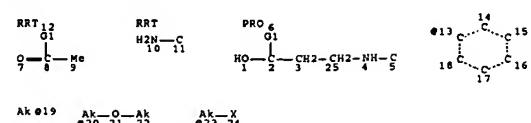
GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE

\*\*\*\*MAPPINGS\*\*\*\*  
 NOD SYM ROL NOD SYM ROL  
 5 C PRO 11 C RRT  
 11 C RRT 5 C PRO  
 L19 150 SEA FILE-CASREACT SSS FUL L15 ( 722 REACTIONS)  
 L24 STR



Ak@19 Ak-O-Ak Ak-X

VAR G1=19/20/23/13

NODE ATTRIBUTES:  
 NSPEC IS RC AT 5  
 NSPEC IS RC AT 11  
 CONNECT IS E1 RC AT 19  
 CONNECT IS E1 RC AT 22  
 DEFAULT MLEVEL IS ATOM  
 MLEVEL IS CLASS AT 1  
 DEFAULT ELEVEL IS LIMITED

GRAPH ATTRIBUTES:  
 RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE

\*\*\*\*MAPPINGS\*\*\*\*  
 NOD SYM ROL NOD SYM ROL  
 5 C PRO 11 C RRT  
 11 C RRT 5 C PRO  
 L27 8 SEA FILE-CASREACT SUB-L19 SSS FUL L24 ( 26 REACTIONS)

100.0% DONE 219 VERIFIED 26 HIT RXNS 8 DOCS

SEARCH TIME: 00.00.03

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L27 ANSWER 1 OF 8 CASREACT COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 146-62451 CASREACT Full-text  
 TITLE: Method for synthesis of 3-methylamino-1-phenylpropanol  
 INVENTOR(S): Yang, Guoming; Huang, Shengjian; Chen, Xia  
 PATENT ASSIGNEE(S): Shangyu Zhongke Baiyun Fine Chemical Research Center Co., Ltd., Peop. Rep. China  
 SOURCE: Faming Zhusnli Shengqing Gongkei Shuomingshu, 10 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Chinese

21

22

CLASSIFICATION: 25-7 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
 FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE  
 CN 1865226 A 20061122 CN 2006-10052037 20060619  
 CN 2006-10052037 20060619  
 PRIORITY APPLN. INFO.:  
 ABSTRACT:  
 The title method comprises the steps: (1) dissolving hypnone, paraformaldehyde and monomethylamine hydrochloride in alc. in an autoclave kettle, heating to 60-100°, concentrating the solution after the reaction, cooling and crystallizing to obtain 3-methylamino-1-phenylpropanol hydrochloride; (2) reducing in the solvent with the catalyst to obtain 3-methylamino-1-phenylpropanol hydrochloride solution; (3) adjusting pH to 9-14 with a base solution, extracting, recycling the solvent and recrystg. with cyclohexane to obtain 3-methylamino-1-phenylpropanol. In step 2, the catalyst is Raney-Ni, the hydrogen pressure = 0.3-1.5 MPa, temperature 25-80°. The method has the advantages of high product yield and quality, low cost and less wastes.

SUPPL. TERM: methylaminophenylpropanol prepn hypnone paraformaldehyde monomethylamine hydrochloride catalytic hydrogenation

INDEX TERM: Hydrogenation  
 (synthesis of methylaminophenylpropanol from hypnone, paraformaldehyde and monomethylamine hydrochloride via catalytic hydrogenation)

INDEX TERM: 7440-02-0, Raney-Nickel, uses

(catalysts; synthesis of methylaminophenylpropanol from hypnone, paraformaldehyde and monomethylamine hydrochloride via catalytic hydrogenation)

INDEX TERM: 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, Isopropanol, uses 110-82-7, Cyclohexane, uses

ROLE: RUU (Other use, unclassified); USES (Uses)  
 (synthesis of methylaminophenylpropanol from hypnone, paraformaldehyde and monomethylamine hydrochloride via catalytic hydrogenation)

INDEX TERM: 98-86-2, Hypnone, reactions 593-51-1, Methylamine hydrochloride 30525-89-4, Paraformaldehyde

ROLE: RCT (Reactant); RACT (Reactant or reagent)  
 (synthesis of methylaminophenylpropanol from hypnone, paraformaldehyde and monomethylamine hydrochloride via catalytic hydrogenation)

INDEX TERM: 2538-50-3P  
 ROLE: RCT (Reactant); SPN (Synthetic preparation); PRSP (Preparation); RACT (Reactant or reagent)

(synthesis of methylaminophenylpropanol from hypnone, paraformaldehyde and monomethylamine hydrochloride via catalytic hydrogenation)

INDEX TERM: 42142-52-9P, 3-Methylamino-1-phenylpropanol

ROLE: SPN (Synthetic preparation); PREP (Preparation)  
 (synthesis of methylaminophenylpropanol from hypnone, paraformaldehyde and monomethylamine hydrochloride via catalytic hydrogenation)

RX(1) OF 3 ...A ===&gt; B

10/520362 10/520362

SOURCE: Angewandte Chemie, International Edition (2005), 44(11), 1687-1689

PUBLISHER: CODEN: ACIEF5; ISSN: 1433-7851

DOCUMENT TYPE: Wiley-VCH Verlag GmbH &amp; Co. KGaA

LANGUAGE: Journal

CLASSIFICATION: English 25-7 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
 Section cross-reference(s): 27

ABSTRACT:  
 Several  $\beta$ -secondary amino ketone hydrochlorides were hydrogenated with remarkably high enantioselectivities by using a rhodium complex containing P-chiral biaphophenole. These results establish a short and practical means for the synthesis of enantiopure N-mono-substituted  $\gamma$ -amino alcohols, which are key intermediates in the synthesis of important antidepressants. For example, the bis[(dimethyl)ethyl]tetra(hydro)-1,1'-bi-1H-isophosphorhodine-rhodium-catalyzed stereoselective hydrogenation of 3-(methylamino)-1-phenyl-1-propanone hydrochloride gave (S)-u-[2-[(methylamino)ethyl]benzenemethanol, which is a synthetic precursor for (S)-N-methyl- $\gamma$ -4-(trifluoromethyl)phenylbenzeneoxapropamine [i.e., (S)-fluoxetine]. The synthesis of (S)-u-[2-[(methylamino)ethyl]thiophenemethanol, a key synthetic intermediate for (S)-duloxetine, was also reported.

SUPPL. TERM: enantiopure aminoalkanol rhodium asym hydrogenation  
 secondary amino ketone; fluoxetine duloxetine asym synthesis  
 hydrogenation amino ketone hydrochloride  
 Alcohol, preparation

INDEX TERM: ROLE: SPN (Synthetic preparation); PREP (Preparation)  
 (aralkyl,  $\alpha$ -(aminoalkyl), chiral; preparation of  
 [(methylamino)ethyl]arenemethanol by  
 tetra(hydro)-1,1'-bi-1H-isophosphorhodine-rhodium-catalyzed  
 stereoselective hydrogenation using  
 (aryl)(methyl)amino)propanone hydrochloride as synthetic  
 intermediate)

INDEX TERM: Alcohol, preparation  
 ROLE: SPN (Synthetic preparation); PREP (Preparation)  
 (benzyl,  $\alpha$ -(aminoalkyl), chiral; preparation of  
 [(methylamino)ethyl]arenemethanol derive. by  
 1,1'-bi-1H-isophosphorhodine-rhodium-catalyzed  
 stereoselective hydrogenation using  
 (aryl)(methyl)amino)propanone hydrochloride as synthetic  
 intermediate)

INDEX TERM: Asymmetric synthesis and induction  
 (preparation of chiral [(methylamino)ethyl]arenemethanol by  
 bis[(dimethyl)ethyl]tetra(hydro)-1,1'-bi-1H-  
 isophosphorhodine-rhodium-catalyzed stereoselective  
 hydrogenation using (aryl)(methyl)amino)propanone  
 hydrochloride as synthetic intermediate)

INDEX TERM: Asymmetric synthesis and induction catalysts  
 (preparation of chiral [(methylamino)ethyl]arenemethanol by  
 tetra(hydro)-1,1'-bi-1H-isophosphorhodine-rhodium-catalyzed  
 stereoselective hydrogenation using  
 (aryl)(methyl)amino)propanone hydrochloride as synthetic  
 intermediate)

INDEX TERM: Hydrogenation  
 Hydrogenation catalysts  
 (stereoselective; preparation of chiral  
 [(methylamino)ethyl]arenemethanol by  
 bis[(dimethyl)ethyl]tetra(hydro)-1,1'-bi-1H-

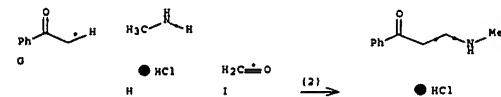
RX(1) RCT A 2538-50-3

STAGE(1)  
 RGT C 1333-74-0 H2  
 CAT 7440-02-0 Ni  
 SOL 7732-18-5 Water  
 CON 70 deg C, 1 MPa

STAGE(2)  
 RGT D 1310-73-2 NaOH  
 SOL 7732-18-5 Water  
 CON pH 11

PRO B 42142-52-9  
 NTE: Raney Nickel used, optimization study, optimized on pH,  
 stoichiometry, pressure, temperature

RX(2) OF 3 G + H + I ===&gt; A...



RX(2) RCT G 98-86-2, H 593-51-1, I 50-00-0

PRO A 2538-50-3  
 SOL 64-17-5 EtOH  
 CON 90 deg C

NTE: Mannich reaction, optimization study, optimized on  
 stoichiometry, temperature, paraformaldehyde used

L27 ANSWER 2 OF 8 CASREACT COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 142-481782 CASREACT Full-text

TITLE: Practical synthesis of enantiopure  $\gamma$ -amino  
 alcohol by rhodium-catalyzed asymmetric hydrogenation -  
 of  $\beta$ -secondary-amino ketones  
 AUTHOR(S): Liu, Duan; Gao, Wenzhong; Wang, Chunjiang; Zhang, Xumu  
 CORPORATE SOURCE: Department of Chemistry, The Pennsylvania State  
 University, University Park, PA, 16802, USA

23

24

INDEX TERM: isophosphindole-rhodium-catalyzed stereoselective hydrogenation using (aryl)({(methyl)amino)propanone hydrochloride as synthetic intermediate)

INDEX TERM: Ketones, preparation

ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

( $\omega$ -amino, hydrochlorides; preparation of [(methyl)amino]ethylarenemethanol by tetra(hydro)-1,1'-bi-1H-isophosphindole-rhodium-catalyzed stereoselective hydrogenation using  $\omega$ -[alkyl]amino ketone hydrochlorides as synthetic intermediates)

INDEX TERM: 116539-59-4P, (S)-Duloxetine

ROLE: SPN (Synthetic preparation); PREP (Preparation) (preparation of (S)-duloxetine using (S)-[(methyl)amino]ethylthiophenemethanol as synthetic intermediate)

INDEX TERM: 100568-02-3P, (S)-Fluoxetine

ROLE: SPN (Synthetic preparation); PREP (Preparation) (preparation of (S)-fluoxetine using (S)-[(methyl)amino]ethylbenzenemethanol as synthetic intermediate)

INDEX TERM: 114133-37-8P

ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of (S)-[(methyl)amino]ethylbenzenemethanol by bis[di(methyl)ethyl]tetra(hydro)-1,1'-bi-1H-isophosphindole-rhodium-catalyzed stereoselective hydrogenation of [(methyl)amino]phenyl-1-propanone hydrochloride)

INDEX TERM: 116539-55-0P

ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of (S)-[(methyl)amino]ethylthiophenemethanol by bis[di(methyl)ethyl]tetra(hydro)-1,1'-bi-1H-isophosphindole-rhodium-catalyzed stereoselective hydrogenation of [(methyl)amino]thiophenyl-1-propanone hydrochloride)

INDEX TERM: 88-15-3, 1-(2-Thienyl)ethanone 93-08-3, 1-(2-Naphthalenyl)ethanone 98-86-2, 1-(Phenyl)ethanone, reactions 99-90-1, 1-(4-Bromophenyl)ethanone 100-06-1, 1-(4-Methoxyphenyl)ethanone 577-16-2, 1-(2-Methylphenyl)ethanone 579-74-8, 1-(2-Methoxyphenyl)ethanone 593-51-1 2142-63-4, 1-(3-Bromophenyl)ethanone 30525-89-4, Paraformaldehyde

ROLE: RCT (Reactant); RACT (Reactant or reagent)

(preparation of [(methyl)amino]aryl-1-propanone hydrochloride using paraformaldehyde, (methyl)amine hydrochloride and (aryl)ethanone as starting materials)

INDEX TERM: 3287-99-8

ROLE: RCT (Reactant); RACT (Reactant or reagent)

(preparation of [(phenyl)methyl]amino)aryl-1-propanone hydrochloride using paraformaldehyde, (benzyl)amine hydrochloride and (aryl)ethanone as starting materials)

INDEX TERM: 35274-92-1P

ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of chiral [(benzyl)amino]ethylarenemethanol by bis[di(methyl)ethyl]tetra(hydro)-1,1'-bi-1H-isophosphindole-rhodium-catalyzed stereoselective

INDEX TERM: 2538-50-3P, 24206-62-0P, 645411-16-1P, 645411-21-8P, 851878-34-9P, 851878-38-1P, 851878-40-5P

ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of chiral [(methyl)amino]ethylarenemethanol by bis[di(methyl)ethyl]tetra(hydro)-1,1'-bi-1H-isophosphindole-rhodium-catalyzed stereoselective hydrogenation using (aryl)({(methyl)amino)propanone hydrochloride as synthetic intermediate)

INDEX TERM: 851878-72-2P, 851878-71-2P, 851878-74-5P, 851878-76-7P, 851878-78-9P, 851878-80-3P, 851878-82-5P, 851878-86-9P

ROLE: SPN (Synthetic preparation); PREP (Preparation) (preparation of chiral [(methyl)amino]ethylarenemethanol by bis[di(methyl)ethyl]tetra(hydro)-1,1'-bi-1H-isophosphindole-rhodium-catalyzed stereoselective hydrogenation using (aryl)({(methyl)amino)propanone hydrochloride as synthetic intermediate)

INDEX TERM: 850780-91-5, 851936-69-1

ROLE: CAT (Catalyst); USES (Uses)

(preparation of chiral  $\gamma$ -amino alc. derivs. by stereoselective hydrogenation of  $\beta$ -secondary amino ketone derivs. using chiral bis[di(methyl)ethyl]tetra(hydro)-1,1'-bi-1H-isophosphindole-rhodium as catalyst)

INDEX TERM: 34597-73-4P

ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of  $\gamma$ -amino alc. derivative by hydrogenation of [(benzyl)amino]aryl-1-propanone hydrochloride derivative)

INDEX TERM: 42142-52-9P, 693261-99-3P, 851878-46-1P, 851878-52-9P

ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

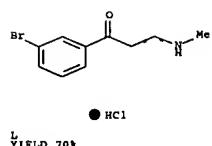
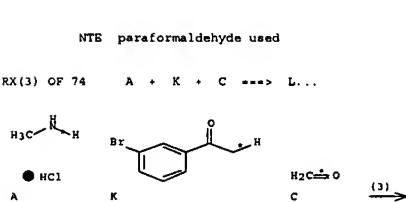
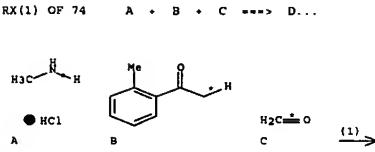
(preparation of  $\gamma$ -amino alc. derivative by hydrogenation of [(methyl)amino]aryl-1-propanone hydrochloride derivative)

INDEX TERM: 851878-69-8P

ROLE: SPN (Synthetic preparation); PREP (Preparation) (preparation of  $\gamma$ -amino alc. derivative by hydrogenation of [(benzyl)amino]aryl-1-propanone hydrochloride derivative)

INDEX TERM: 116539-56-1P, 851878-48-3P, 851878-50-7P, 851878-54-1P, 851878-58-5P, 851878-62-1P, 851878-65-4P, 851878-67-6P

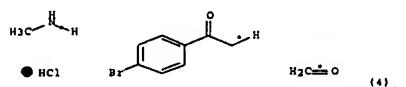
ROLE: SPN (Synthetic preparation); PREP (Preparation) (preparation of  $\gamma$ -amino alc. derivative by hydrogenation of [(methyl)amino]aryl-1-propanone hydrochloride derivative)



STAGE(1)  
RCT E 7647-01-0 HCl  
SOL 7732-18-5 Water, 64-17-5 EtOH  
CON SUBSTAGE(1) 9 - 20 hours, 110 deg C  
SUBSTAGE(2) 110 deg C  $\rightarrow$  room temperature

STAGE(2)  
SOL 141-78-6 AcOEt  
CON 4 hours, room temperature

PRO L 851878-36-9  
NTE paraformaldehyde used



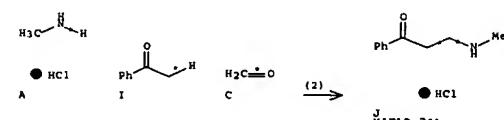
RX(1) RCT A 593-51-1, B 577-16-2, C 50-00-0

STAGE(1)  
RCT E 7647-01-0 HCl  
SOL 7732-18-5 Water, 64-17-5 EtOH  
CON SUBSTAGE(1) 9 - 20 hours, 110 deg C  
SUBSTAGE(2) 110 deg C  $\rightarrow$  room temperature

STAGE(2)  
SOL 141-78-6 AcOEt  
CON 4 hours, room temperature

PRO D 851878-34-7  
NTE paraformaldehyde used

RX(2) OF 74 A + I + C  $\rightarrow$  J...

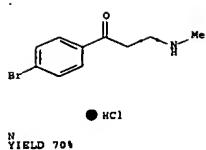


RX(2) RCT A 593-51-1, I 98-86-2, C 50-00-0

STAGE(1)  
RCT E 7647-01-0 HCl  
SOL 7732-18-5 Water, 64-17-5 EtOH  
CON SUBSTAGE(1) 9 - 20 hours, 110 deg C  
SUBSTAGE(2) 110 deg C  $\rightarrow$  room temperature

STAGE(2)  
SOL 141-78-6 AcOEt  
CON 4 hours, room temperature

PRO J 2538-50-3



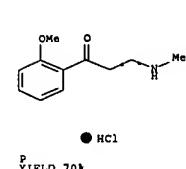
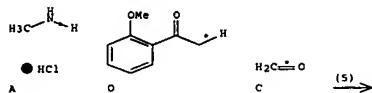
RX(4) RCT A 593-51-1, M 99-90-1, C 50-00-0

STAGE(1)  
RGT E 7647-01-0 HCl  
SOL 7732-18-5 Water, 64-17-5 EtOH  
CON SUBSTAGE(1) 9 - 20 hours, 110 deg C  
SUBSTAGE(2) 110 deg C -> room temperature

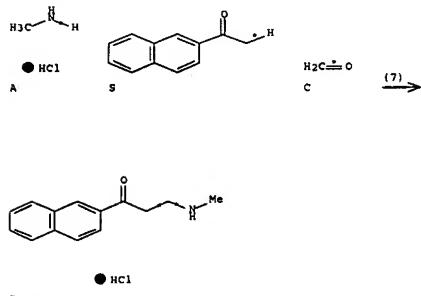
STAGE(2)  
SOL 141-78-6 AcOEt  
CON 4 hours, room temperature

PRO N 851878-38-1  
NTS paraformaldehyde used

RX(5) OF 74 A + O + C ==&gt; P...



RX(7) OF 74 A + S + C ==&gt; T...



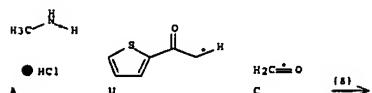
RX(7) RCT A 593-51-1, S 93-08-3, C 50-00-0

STAGE(1)  
RGT E 7647-01-0 HCl  
SOL 7732-18-5 Water, 64-17-5 EtOH  
CON SUBSTAGE(1) 9 - 20 hours, 110 deg C  
SUBSTAGE(2) 110 deg C -> room temperature

STAGE(2)  
SOL 141-78-6 AcOEt  
CON 4 hours, room temperature

PRO T 645411-21-8  
NTS paraformaldehyde used

RX(8) OF 74 A + U + C ==&gt; V...



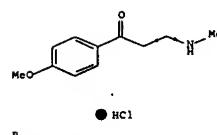
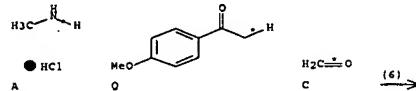
RX(5) RCT A 593-51-1, O 579-74-8, C 50-00-0

STAGE(1)  
RGT E 7647-01-0 HCl  
SOL 7732-18-5 Water, 64-17-5 EtOH  
CON SUBSTAGE(1) 9 - 20 hours, 110 deg C  
SUBSTAGE(2) 110 deg C -> room temperature

STAGE(2)  
SOL 141-78-6 AcOEt  
CON 4 hours, room temperature

PRO P 851878-40-5  
NTS paraformaldehyde used

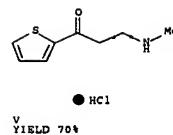
RX(6) OF 74 A + O + C ==&gt; R...



RX(6) RCT A 593-51-1, Q 100-06-1, C 50-00-0

STAGE(1)  
RGT E 7647-01-0 HCl  
SOL 7732-18-5 Water, 64-17-5 EtOH  
CON SUBSTAGE(1) 9 - 20 hours, 110 deg C  
SUBSTAGE(2) 110 deg C -> room temperature

STAGE(2)  
SOL 141-78-6 AcOEt  
CON 4 hours, room temperature

PRO R 24206-62-0  
NTS paraformaldehyde used

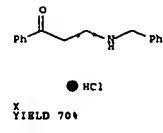
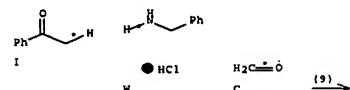
RX(8) RCT A 593-51-1, U 88-15-3, C 50-00-0

STAGE(1)  
RGT E 7647-01-0 HCl  
SOL 7732-18-5 Water, 64-17-5 EtOH  
CON SUBSTAGE(1) 9 - 20 hours, 110 deg C  
SUBSTAGE(2) 110 deg C -> room temperature

STAGE(2)  
SOL 141-78-6 AcOEt  
CON 4 hours, room temperature

PRO V 645411-16-1  
NTS paraformaldehyde used

RX(9) OF 74 I + W + C ==&gt; X...



RX(9) RCT I 98-86-2, W 3287-99-8, C 50-00-0

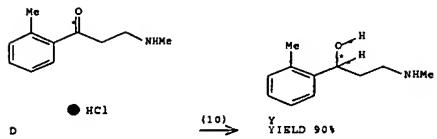
STAGE(1)  
RGT E 7647-01-0 HCl

SOL 7732-18-5 Water, 64-17-5 EtOH  
CON SUBSTAGE(1) 9 - 20 hours, 110 deg C  
SUBSTAGE(2) 110 deg C -> room temperature

STAGE(2)  
SOL 141-78-6 AcOEt  
CON 4 hours, room temperature

PRO X 35274-92-1  
NTB paraformaldehyde used

RX(10) OF 74 ...D ==> Y...



RX(10) RCT D 851878-34-7

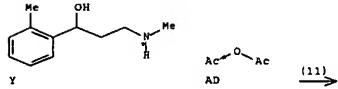
STAGE(1)  
RGT Z 16940-66-2 NaBH4  
SOL 67-56-1 MeOH  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 1 hour, room temperature

STAGE(2)  
RGT AA 12125-02-9 NH4Cl  
SOL 7732-18-5 Water  
CON room temperature

STAGE(3)  
RGT AB 1310-73-2 NaOH  
SOL 7732-18-5 Water  
CON room temperature, basify

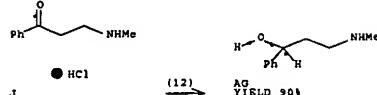
PRO Y 851878-46-1

RX(11) OF 74 ...Y + AD ==> AE



RX(11) RCT Y 851878-46-1, AD 108-24-7  
PRO AE 851878-48-3  
SOL 75-09-2 CH2Cl2  
CON 10 minutes, 0 deg C

RX(12) OF 74 ...J ==> AG...



RX(12) RCT J 2538-50-3

STAGE(1)  
RGT Z 16940-66-2 NaBH4  
SOL 67-56-1 MeOH  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 1 hour, room temperature

STAGE(2)  
RGT AA 12125-02-9 NH4Cl  
SOL 7732-18-5 Water  
CON room temperature

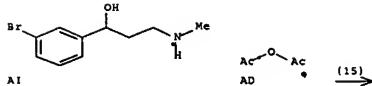
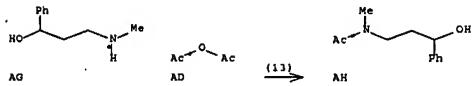
STAGE(3)  
RGT AB 1310-73-2 NaOH  
SOL 7732-18-5 Water  
CON room temperature, basify

PRO AG 42142-52-9

RX(13) OF 74 ...AG + AD ==> AH

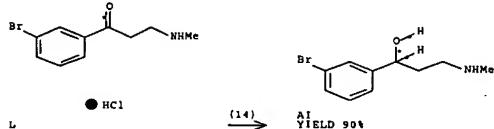
33

34



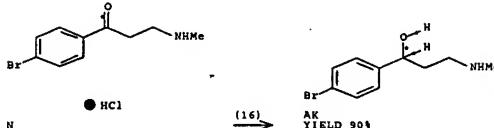
RX(13) RCT AG 42142-52-9, AD 108-24-7  
PRO AH 851878-50-7  
SOL 75-09-2 CH2Cl2  
CON 10 minutes, 0 deg C

RX(14) OF 74 ...L ==> AI...



RX(15) RCT AI 851878-52-9, AD 108-24-7  
PRO AJ 851878-54-1  
SOL 75-09-2 CH2Cl2  
CON 10 minutes, 0 deg C

RX(16) OF 74 ...N ==> AK...



RX(16) RCT N 851878-38-1

STAGE(1)  
RGT Z 16940-66-2 NaBH4  
SOL 67-56-1 MeOH  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 1 hour, room temperature

STAGE(2)  
RGT AA 12125-02-9 NH4Cl  
SOL 7732-18-5 Water  
CON room temperature

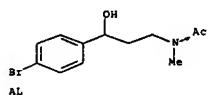
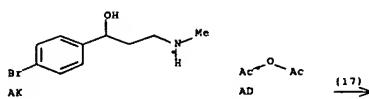
STAGE(3)  
RGT AB 1310-73-2 NaOH

RX(15) OF 74 ...AI + AD ==> AJ

SOL 7732-18-5 Water  
CON room temperature, basify

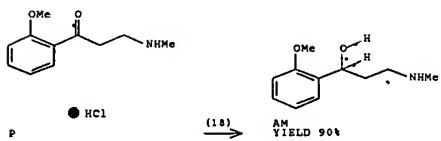
PRO AK 851878-56-3

RX(17) OF 74 ...AK + AD ===&gt; AL



RX(17) RCT AK 851878-56-3, AD 108-24-7  
PRO AL 851878-58-5  
SOL 75-09-2 CH2Cl2  
CON 10 minutes, 0 deg C

RX(18) OF 74 ...P ===&gt; AM...



RX(18) RCT P 851878-40-5

STAGE(1)  
RGT Z 16940-66-2 NaBH4  
SOL 67-56-1 MeOH  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 1 hour, room temperature

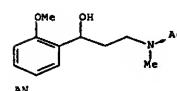
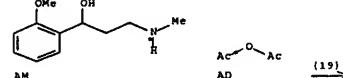
37

38

STAGE(2)  
RGT AA 12125-02-9 NH4Cl  
SOL 7732-18-5 Water  
CON room temperature  
STAGE(3)  
RGT AB 1310-73-2 NaOH  
SOL 7732-18-5 Water  
CON room temperature, basify

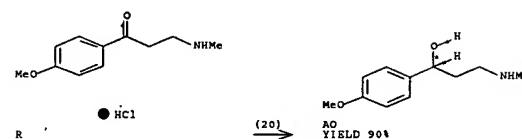
PRO AM 851878-60-9

RX(19) OF 74 ...AM + AD ===&gt; AN



RX(19) RCT AM 851878-60-9, AD 108-24-7  
PRO AN 851878-62-1  
SOL 75-09-2 CH2Cl2  
CON 10 minutes, 0 deg C

RX(20) OF 74 ...R ===&gt; AO...

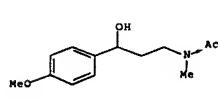
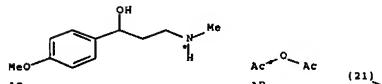


RX(20) RCT R 24206-62-0

STAGE(1)  
RGT Z 16940-66-2 NaBH4  
SOL 67-56-1 MeOH  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 1 hour, room temperature  
STAGE(2)  
RGT AA 12125-02-9 NH4Cl  
SOL 7732-18-5 Water  
CON room temperature  
STAGE(3)  
RGT AB 1310-73-2 NaOH  
SOL 7732-18-5 Water  
CON room temperature, basify

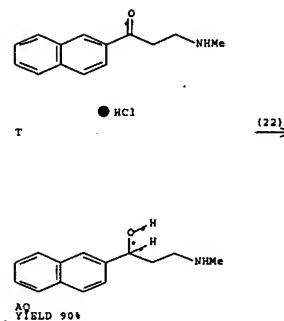
PRO AO 693261-99-3

RX(21) OF 74 ...AO + AD ===&gt; AP



RX(21) RCT AO 693261-99-3, AD 108-24-7  
PRO AP 851878-65-4  
SOL 75-09-2 CH2Cl2  
CON 10 minutes, 0 deg C

RX(22) OF 74 ...T ===&gt; AQ



RX(22) RCT T 645411-21-8

STAGE(1)  
RGT Z 16940-66-2 NaBH4  
SOL 67-56-1 MeOH  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 1 hour, room temperature  
STAGE(2)  
RGT AA 12125-02-9 NH4Cl  
SOL 7732-18-5 Water  
CON room temperature  
STAGE(3)  
RGT AB 1310-73-2 NaOH  
SOL 7732-18-5 Water  
CON room temperature, basify

PRO AQ 851878-67-6

RX(23) OF 74 ...V ===&gt; AR



39

40

RX(23) RCT V 645411-16-1

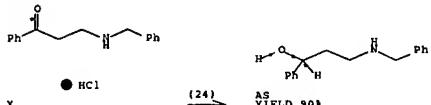
STAGE(1)  
 RGT Z 16940-66-2 NaBH4  
 SOL 67-56-1 MeOH  
 CON SUBSTAGE(1) room temperature  
 SUBSTAGE(2) 1 hour, room temperature

STAGE(2)  
 RGT AA 12125-02-9 NH4Cl  
 SOL 7732-18-5 Water  
 CON room temperature

STAGE(3)  
 RGT AB 1310-73-2 NaOH  
 SOL 7732-18-5 Water  
 CON room temperature, basify

PRO AR 116539-56-1

RX(24) OF 74 ...X ==&gt; AS...



RX(24) RCT X 35274-92-1

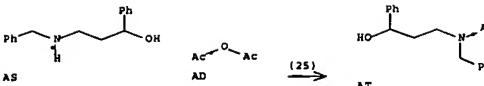
STAGE(1)  
 RGT Z 16940-66-2 NaBH4  
 SOL 67-56-1 MeOH  
 CON SUBSTAGE(1) room temperature  
 SUBSTAGE(2) 1 hour, room temperature

STAGE(2)  
 RGT AA 12125-02-9 NH4Cl  
 SOL 7732-18-5 Water  
 CON room temperature

STAGE(3)  
 RGT AB 1310-73-2 NaOH  
 SOL 7732-18-5 Water  
 CON room temperature, basify

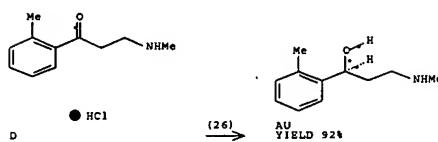
PRO AS 34597-73-4

RX(25) OF 74 ...AS + AD ==&gt; AT



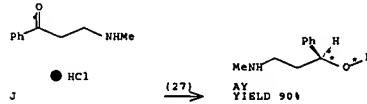
RX(25) RCT AS 34597-73-4, AD 108-24-7  
 PRO AT 851878-69-8  
 SOL 75-09-2 CH2Cl2  
 CON 10 minutes, 0 deg C

RX(26) OF 74 ...D ==&gt; AU



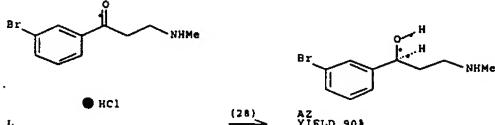
RX(26) RCT D 851878-34-7  
 RGT AV 584-08-7 K2CO3, AW 1333-74-0 H2  
 PRO AU 851878-71-2  
 CAT 851936-69-1 Rhodium(1+), [(2,3,5,6-η)-bicyclo[2.2.1]hepta-2,5-diene][(1S,1'S,2S,2'S)-2,2'-bis(1,1-dimethylethyl)-2,2',3,3'-tetrahydro-1,1'-bi-1H-isophosphindole-κP2,κP2']-, (OC-6-11)-hexafluoroantimonate(1-)  
 SOL 67-56-1 MeOH  
 CON 12 hours, 50 deg C, 10 bar  
 NTE stereoselective, optimization study (optimized on reagent, solvent, pressure)

RX(27) OF 74 ...J ==&gt; AY...



RX(27) RCT J 2538-50-3  
 RGT AV 584-08-7 K2CO3, AW 1333-74-0 H2  
 PRO J 114133-37-8  
 CAT 851936-69-1 Rhodium(1+), [(2,3,5,6-η)-bicyclo[2.2.1]hepta-2,5-diene][(1S,1'S,2S,2'S)-2,2'-bis(1,1-dimethylethyl)-2,2',3,3'-tetrahydro-1,1'-bi-1H-isophosphindole-κP2,κP2']-, (OC-6-11)-hexafluoroantimonate(1-)  
 SOL 67-56-1 MeOH  
 CON 12 hours, 50 deg C, 10 bar  
 NTE stereoselective

RX(28) OF 74 ...L ==&gt; AZ



RX(28) RCT L 851878-36-9  
 RGT AV 584-08-7 K2CO3, AW 1333-74-0 H2  
 PRO AZ 851878-74-5

CAT 851936-69-1 Rhodium(1+), [(2,3,5,6-η)-bicyclo[2.2.1]hepta-2,5-diene][(1S,1'S,2S,2'S)-2,2'-bis(1,1-dimethylethyl)-2,2',3,3'-tetrahydro-1,1'-bi-1H-isophosphindole-κP2,κP2']-, (OC-6-11)-hexafluoroantimonate(1-)  
 SOL 67-56-1 MeOH  
 CON 12 hours, 50 deg C, 10 bar  
 NTE stereoselective

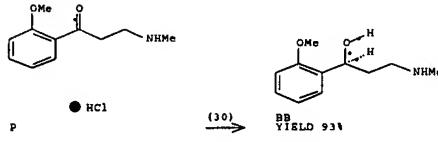
RX(29) OF 74 ...N ==&gt; BA



RX(29) RCT N 851878-38-1  
 RGT AV 584-08-7 K2CO3, AW 1333-74-0 H2

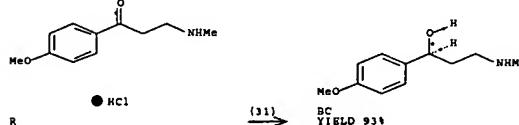
PRO BA 851878-76-7  
 CAT 851926-69-1 Rhodium(1+), [(2,3,5,6-η)-bicyclo[2.2.1]hepta-2,5-diene][(1S,1'S,2S,2'S)-2,2'-bis(1,1-dimethylethyl)-2,2',3,3'-tetrahydro-1,1'-bi-1H-isophosphindole-κP2,κP2']-, (OC-6-11)-hexafluoroantimonate(1-)  
 SOL 67-56-1 MeOH  
 CON 12 hours, 50 deg C, 10 bar  
 NTE stereoselective

RX(30) OF 74 ...P ==&gt; BB



RX(30) RCT P 851878-40-5  
 RGT AV 584-08-7 K2CO3, AW 1333-74-0 H2  
 PRO BB 851878-78-9  
 CAT 851936-69-1 Rhodium(1+), [(2,3,5,6-η)-bicyclo[2.2.1]hepta-2,5-diene][(1S,1'S,2S,2'S)-2,2'-bis(1,1-dimethylethyl)-2,2',3,3'-tetrahydro-1,1'-bi-1H-isophosphindole-κP2,κP2']-, (OC-6-11)-hexafluoroantimonate(1-)  
 SOL 67-56-1 MeOH  
 CON 12 hours, 50 deg C, 10 bar  
 NTE stereoselective

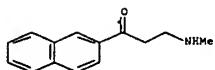
RX(31) OF 74 ...R ==&gt; BC



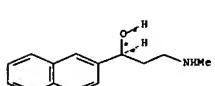
RX(31) RCT R 24206-62-0  
 RGT AV 584-08-7 K2CO3, AW 1333-74-0 H2  
 PRO BC 851878-80-3  
 CAT 851936-69-1 Rhodium(1+), [(2,3,5,6-η)-bicyclo[2.2.1]hepta-2,5-diene][(1S,1'S,2S,2'S)-2,2'-bis(1,1-dimethylethyl)-2,2',3,3'-tetrahydro-1,1'-bi-1H-isophosphindole-κP2,κP2']-, (OC-6-11)-hexafluoroantimonate(1-)

(OC-6-11)-hexafluoroantimonate(1-)  
 SOL 67-56-1 MeOH  
 CON 12 hours, 50 deg C, 10 bar  
 NTE stereoselective

RX(32) OF 74 ...T ==> BD



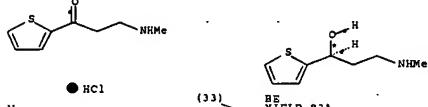
T  $\xrightarrow{(32)}$



BD YIELD 92%

RX(32) RCT T 645411-21-8  
 RGT AV 584-08-7 K2CO3, AW 1333-74-0 H2  
 PRO BD 851878-82-5  
 CAT 851936-69-1 Rhodium(1+), [(2,3,5,6-η)-bicyclo[2.2.1]hepta-2,5-diene][(1S,1'S,2S,2'S)-2,2'-bis(1,1-dimethylethyl)-2,2',3,3'-tetrahydro-1,1'-bi-1H-isophosphindole-κP2,κP2']-, (OC-6-11)-hexafluoroantimonate(1-)  
 SOL 67-56-1 MeOH  
 CON 12 hours, 50 deg C, 10 bar  
 NTE stereoselective

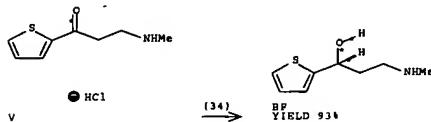
RX(33) OF 74 ...V ==> BE...



V  $\xrightarrow{(33)}$  BE YIELD 93%

RX(33) RCT V 645411-16-1  
 RGT AV 584-08-7 K2CO3, AW 1333-74-0 H2  
 PRO BS 116539-55-0  
 CAT 851936-69-1 Rhodium(1+), [(2,3,5,6-η)-bicyclo[2.2.1]hepta-2,5-diene][(1S,1'S,2S,2'S)-2,2'-bis(1,1-dimethylethyl)-2,2',3,3'-tetrahydro-1,1'-bi-1H-isophosphindole-κP2,κP2']-, (OC-6-11)-hexafluoroantimonate(1-)  
 SOL 67-56-1 MeOH  
 CON 12 hours, 50 deg C, 10 bar  
 NTE stereoselective

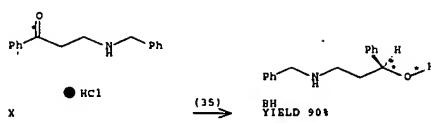
RX(34) OF 74 ...V ==> BF



V  $\xrightarrow{(34)}$  BF YIELD 93%

RX(34) RCT V 645411-16-1  
 RGT AV 584-08-7 K2CO3, AW 1333-74-0 H2  
 PRO BF 116539-57-2  
 CAT 850780-91-5 Rhodium(1+), [(2,3,5,6-η)-bicyclo[2.2.1]hepta-2,5-diene][(1R,1'R,2R,2'R)-2,2'-bis(1,1-dimethylethyl)-2,2',3,3'-tetrahydro-1,1'-bi-1H-isophosphindole-κP2,κP2']-, (OC-6-11)-hexafluoroantimonate(1-)  
 SOL 67-56-1 MeOH  
 CON 12 hours, 50 deg C, 10 bar  
 NTE stereoselective

RX(35) OF 74 ...X ==> BH



X  $\xrightarrow{(35)}$  BH YIELD 90%

RX(35) RCT X 35274-92-1  
 RGT AV 584-08-7 K2CO3, AW 1333-74-0 H2  
 PRO BH 851878-86-9  
 CAT 851936-69-1 Rhodium(1+), [(2,3,5,6-η)-bicyclo[2.2.1]hepta-

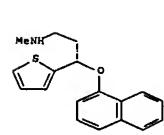
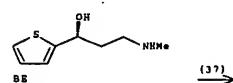
2,5-diene][(1S,1'S,2S,2'S)-2,2'-bis(1,1-dimethylethyl)-2,2',3,3'-tetrahydro-1,1'-bi-1H-isophosphindole-κP2,κP2']-, (OC-6-11)-hexafluoroantimonate(1-)  
 SOL 67-56-1 MeOH  
 CON 12 hours, 50 deg C, 10 bar  
 NTE stereoselective

RX(36) OF 74 ...AY ==> BI



RX(36) RCT AV 114133-37-8  
 PRO BI 100568-02-3  
 NTE literature preparation

RX(37) OF 74 ...BE ==> BJ



RX(37) RCT BE 116539-55-0  
 PRO BJ 116539-59-4  
 NTE literature preparation

PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA  
 SOURCE: U.S. Pat. Appl. Publ., 7 pp.

DOCUMENT TYPE: Patent  
 CODEN: USXXCO

LANGUAGE: English

INT. PATENT CLASSIF.: C07C225-10

US PATENT CLASSIF.: 564343000

CLASSIFICATION: 25-9 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
 Section cross-reference(s): 45, 63

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004102651	A1	20040527	US 2002-302806	20021122
US 6846957	B2	20050125		

PRIORITY APPLN. INFO.: US 2002-302806 20021122

ABSTRACT:

Fluoxetine hydrochloride is prepared by: (a) synthesizing 1-phenyl-3-methylamino-1-propan-1-one by (i) the claisen condensation of acetophenone with Et formate leading to benzylacetalddehyde sodium salt, and (ii) the condensation of benzylacetalddehyde sodium salt with methylamine hydrochloride; (b) converting 1-phenyl-3-methylamino-1-propan-1-one into 3-methylamino-1-phenyl-1-propanol using sodium borohydride and acetic acid; and (c) converting 3-methylamino-1-phenyl-1-propanol into fluoxetine hydrochloride by treatment with hydrochloric acid.

SUPPL. TERM: fluoxetine hydrochloride prep; aminomethylpropanol prep  
 INDEX TERM: Condensation reaction  
 (Claisen; of acetophenone with Et formate to give benzylacetalddehyde sodium salt)

INDEX TERM: Reduction  
 (of 1-phenyl-3-methylamino-1-propan-1-one into 3-methylamino-1-phenyl-1-propanol with NaBH4 in AcOH)

INDEX TERM: Condensation reaction  
 (of benzylacetalddehyde sodium salt with methylamine hydrochloride to give 1-phenyl-3-methylamino-1-propan-1-one)

INDEX TERM: Neutralization  
 (of fluoxetine with HCl in ether in the preparation of fluoxetine hydrochloride)

INDEX TERM: Ethers, uses

ROLE: NUU (Other use, unclassified); USES (Uses)  
 (solvents; for the salification of fluoxetine with HCl)

INDEX TERM: 64-19-7, Acetic acid, uses

ROLE: NUU (Other use, unclassified); USES (Uses)  
 (in the preparation of fluoxetine hydrochloride)

INDEX TERM: 98-56-6, 4-Chlorobenzotrifluoride, 98-86-2, Acetophenone, reactions 109-94-4, Ethyl formate, 593-51-1, Methylamine hydrochloride, 1310-73-2, Sodium hydroxide, reactions 7647-01-0, Hydrogen chloride, reactions 16940-66-2, Sodium borohydride

ROLE: RCT (Reactant); RACT (Reactant or reagent)  
 (in the preparation of fluoxetine hydrochloride)

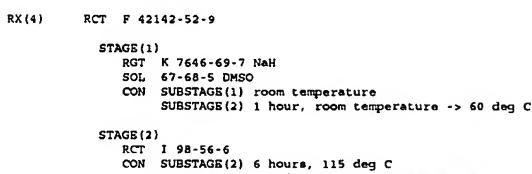
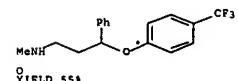
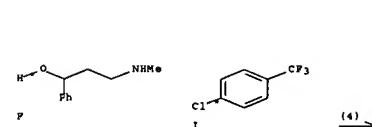
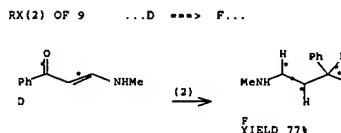
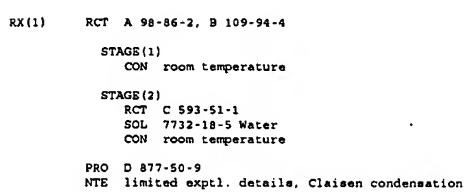
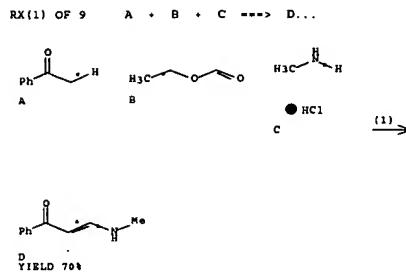
INDEX TERM: 877-59-9P, 2017-88-2, Benzylacetalddehyde sodium salt 42142-52-9P, 3-Methylamino-1-phenyl-1-propanol

ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

INDEX TERM: (in the preparation of fluoxetine hydrochloride)  
54910-89-3P  
ROLE: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)  
INDEX TERM: 56296-78-7P, Fluoxetine hydrochloride  
ROLE: SPN (Synthetic preparation); THU (Therapeutic use);  
BIOL (Biological study); PREP (Preparation); USSS (Uses)  
(preparation of)  
INDEX TERM: 67-68-5, Dmso, uses  
ROLE: MUJ (Other use, unclassified); USSS (Uses)  
(solvent; in the preparation of fluoxetine hydrochloride)  
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD.

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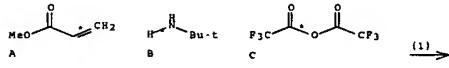


L27 ANSWER 4 OF 8 CASREACT COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 114:5913 CASREACT Full-text  
TITLE: Synthesis of tritium labeled 1-(3,4-dichlorophenyl)-3-(methylamino)propanol hydrochloride  
AUTHOR(S): Hill, John A.; Wisowaty, James C.  
CORPORATE SOURCE: Chem. Dev. Lab., Burroughs Wellcome Co., Research Triangle Park, NC, 27709, USA  
SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals (1990), 28(7), 811-18  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
CLASSIFICATION: 25-7 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
GRAPHIC IMAGE:



INDEX TERM: ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and addition reaction of, with hydroxybutene)  
111525-42-9P  
INDEX TERM: ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and addition reactions of, with allylic alcs.)  
56816-01-4P  
INDEX TERM: ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and amidation of)  
111525-44-1P 111525-45-2P 111525-46-3P 111525-48-5P  
111612-96-5P  
INDEX TERM: ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and asyrm. carbanion accelerated Claisen rearrangement of)  
111525-40-7P  
INDEX TERM: ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and borane reduction of)  
111525-38-3P  
INDEX TERM: ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and reaction of, with Grignard reagent)  
111525-41-8P  
INDEX TERM: ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and reaction of, with trichlorophosphine and hydroxybutene, allenylphosphoramides from)  
111525-50-9P 111525-53-2P 111612-97-6P 111612-98-7P  
111612-99-8P 111613-00-4P 111613-02-6P  
INDEX TERM: ROLE: SPN (Synthetic preparation); PREP (Preparation) (preparation of)  
7719-12-2, Trichlorophosphine  
INDEX TERM: ROLE: RCT (Reactant); RACT (Reactant or reagent) (reaction of, with amino alcs. and propargyl alcs., allenylphosphoramides from)  
115-19-5  
INDEX TERM: ROLE: RCT (Reactant); RACT (Reactant or reagent) (reaction of, with trichlorophosphine and amino alc., allenylphosphoramide from)  
2028-63-9, 3-Hydroxy-1-butene  
INDEX TERM: ROLE: RCT (Reactant); RACT (Reactant or reagent) (reaction of, with trichlorophosphine and amino alcs., allenylphosphoramides from)  
111525-39-4  
INDEX TERM: ROLE: RCT (Reactant); RACT (Reactant or reagent) (reaction of, with trichlorophosphine and propargyl alc., allenylphosphoramide from)

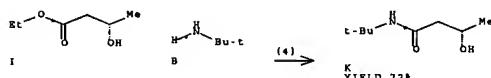
RX(1) OF 80 A + B + C ==&gt; D...



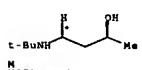
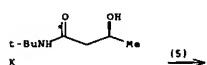
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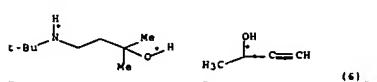
RX(4) OF 80 ...I + B ==&gt; K...

RX(4) RCT I 56816-01-4, B 75-64-9  
RGT L 75-24-1 AlMe3  
PRO K 111525-40-7

RX(5) OF 80 ...K ==&gt; M...

RX(5) RCT K 111525-40-7  
RGT N 14044-65-6 BH3-THF  
PRO M 111525-41-8

RX(6) OF 80 ...E + O ==&gt; P...

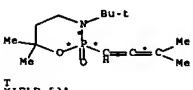
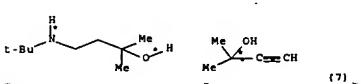


RX(2) RCT D 111525-38-3  
RGT F 75-16-1 MeMgBr  
PRO E 111525-39-4  
SOL 60-29-7 Et2O

RX(3) RCT H 141-97-9  
PRO I 56816-01-4  
SOL 7732-18-5 Water  
NTE yeast

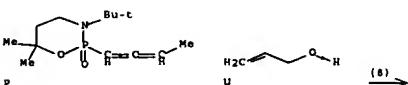
RX(6) RCT E 111525-39-4, O 2028-63-9  
RGT Q 109-02-4 N-Methylmorpholine, R 7719-12-2 PC13  
PRO P 111525-42-9

RX(7) OF 80 ...E + S ==&gt; T...



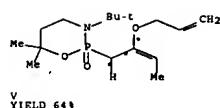
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RGT O 109-02-4 N-Methylmorpholine, R 7719-12-2 PC13  
PRO T 111525-43-0

RX(8) OF 80 ...P + U ==&gt; V...

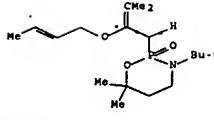


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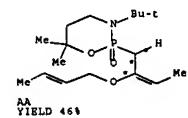
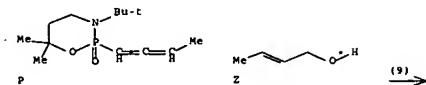
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RX(8) RCT P 111525-42-9, U 107-18-6  
RGT W 7646-69-7 NaH, X 75-65-0 t-BuOH  
PRO V 111525-44-1  
SOL 109-99-9 THF

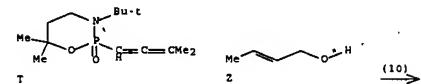


RX(9) OF 80 ...P + Z ==> AA...



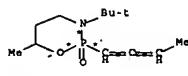
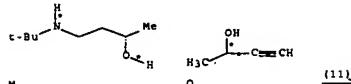
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RGT W 7646-69-7 NaH, X 75-65-0 t-BuOH  
PRO AA 111525-45-2  
SOL 109-99-9 THF

RX(10) OF 80 ...T + Z ==> AB...



RX(10) RCT T 111525-43-0, Z 504-61-0  
RGT W 7646-69-7 NaH, X 75-65-0 t-BuOH  
PRO AB 111525-46-3  
SOL 109-99-9 THF

RX(11) OF 80 ...M + O ==> AC...

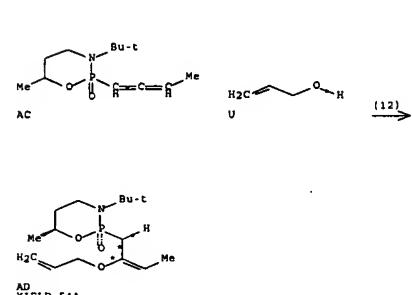


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RGT O 109-02-4 N-Methylmorpholine, R 7719-12-2 PC13  
PRO AC 111525-47-4

RX(12) OF 80 ...AC + U ==> AD...

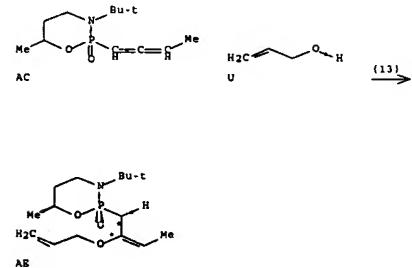
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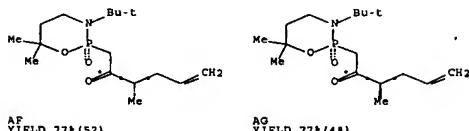
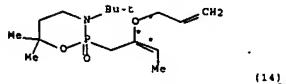
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PRO AD 111525-48-5  
SOL 109-99-9 THF

RX(13) OF 80 ...AC + U ==> AE...



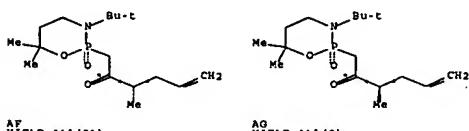
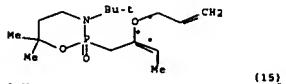
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RGT W 7646-69-7 NaH, X 75-65-0 t-BuOH  
PRO AE 111612-96-5  
SOL 109-99-9 THF

RX(14) OF 80 ...2 V ==> AF + AG



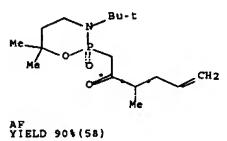
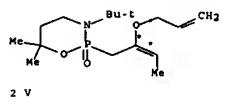
RX(14) RCT V 111525-44-1  
RGT AH 7693-26-7 KH  
PRO AF 111525-49-6, AG 111525-50-9  
SOL 67-68-5 DMSO, 109-99-9 THF

RX(15) OF 80 2 V ==> AF + AG



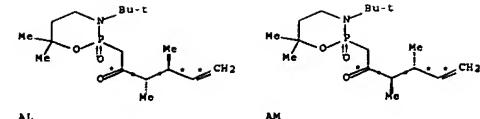
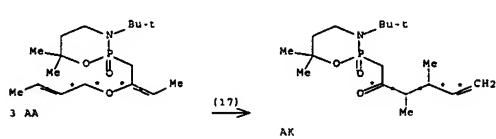
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RGT AH 7693-26-7 KH, AJ 7447-41-8 LiCl  
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SOL 67-68-5 DMSO, 109-99-9 THF

RX(16) OF 80 2 V ==> AF + AG



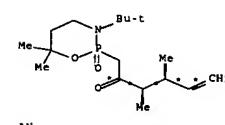
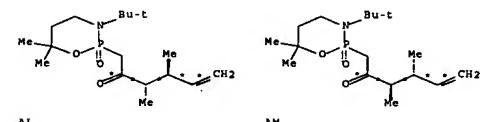
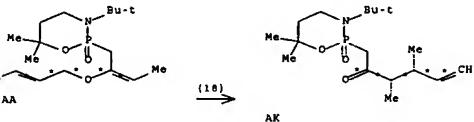
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SOL 109-99-9 THF

RX(17) OF 80 ...3 AA ==> AK + AL + AM



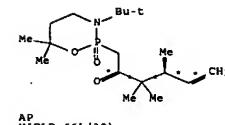
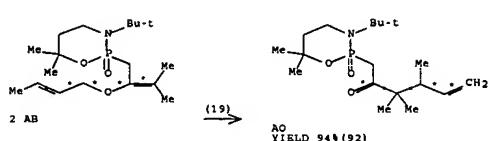
RX(17) RCT AA 111525-45-2  
RGT AH 7693-26-7 KH, AJ 7447-41-8 LiCl  
PRO AK 111525-51-0, AL 111612-97-6, AM 111612-98-7  
SOL 67-68-5 DMSO, 109-99-9 THF  
NTB 80% overall

RX(18) OF 80 ...4 AA ==> AK + AL + AM + AN



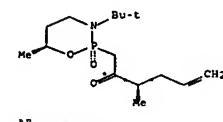
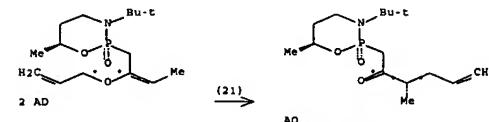
RX(18) RCT AA 111525-45-2  
PRO AK 111525-51-0, AL 111612-97-6, AM 111612-98-7, AN 111612-99-8  
SOL 109-99-9 THF  
NTB 84% overall

RX(19) OF 80 ...2 AB ==> AO + AP



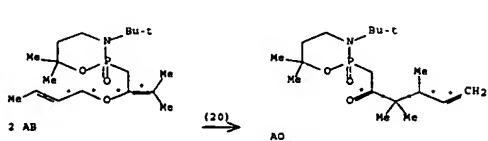
RX(20) RCT AB 111525-46-3  
PRO AO 111525-52-1, AP 111525-53-2  
SOL 109-99-9 THF

RX(21) OF 80 ...2 AD ==> AQ + AR



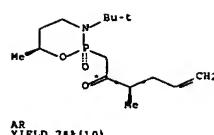
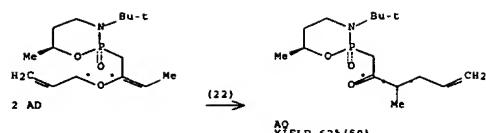
RX(19) RCT AB 111525-46-3  
RGT AH 7693-26-7 KH, AJ 7447-41-8 LiCl  
PRO AO 111525-52-1, AP 111525-53-2  
SOL 67-68-5 DMSO, 109-99-9 THF

RX(20) OF 80 2 AB ==> AO + AP



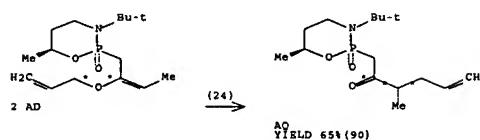
RX(21) RCT AD 111525-48-5  
RGT AJ 7447-41-8 LiCl  
PRO AR 111525-54-3, AR 111613-00-4  
SOL 109-99-9 THF

RX(22) OF 80 2 AD ==> AQ + AR



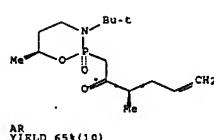
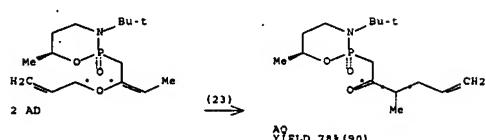
RX(23) RCT AD 111525-48-5  
RG RT AH 7693-26-7 KH  
PRO AQ 111525-54-3, AR 111613-00-4  
SOL 67-68-5 DMSO, 109-99-9 THF

RX(24) OF 80 2 AD ==> AQ + AR



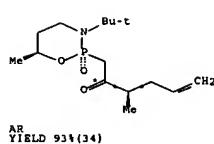
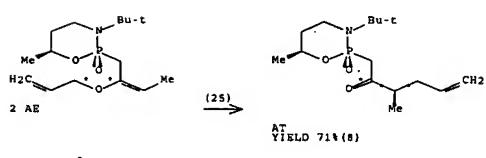
RX(22) RCT AD 111525-48-5  
RG RT AH 7693-26-7 KH  
PRO AQ 111525-54-3, AR 111613-00-4  
SOL 67-68-5 DMSO, 109-99-9 THF

RX(23) OF 80 2 AD ==> AQ + AR



RX(24) RCT AD 111525-48-5  
RG RT AS 109-72-8 BuLi  
PRO AQ 111525-54-3, AR 111613-00-4  
SOL 67-68-5 DMSO, 109-99-9 THF

RX(25) OF 80 ... 2 AB ==> AT + AU



RX(26) RCT AD 111525-48-5  
PRO AQ 111525-54-3, AR 111613-00-4  
SOL 109-99-9 THF

L27 ANSWER 6 OF 8 CASREACT COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 102:46134 CASREACT Full-text  
TITLE: Herbicidal  $\alpha$ -hydroxy phosphonates  
INVENTOR(S): Gaertner, Van R.  
PATENT ASSIGNEE(S): Monsanto Co., USA  
SOURCE: U.S., 9 pp. Division of U.S. 4,413,125.  
CODEN: USXXAM

DOCUMENT TYPE: Patent  
LANGUAGE: English  
INT. PATENT CLASSIF.: A01N057-20  
US PATENT CLASSIF.: 07108600  
CLASSIFICATION: 29- (Organometallic and Organometalloidal Compounds)  
Section cross-reference(s): 5  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4475943	A	19841009	US 1983-528700	19830901
US 4413125	A	19831101	US 1981-279371	19810701

PRIORITY APPLN. INFO.: US 1981-279371 19810701

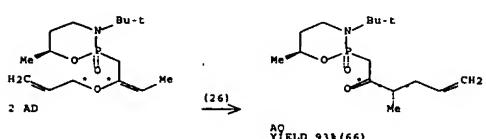
OTHER SOURCE(S): MARPAT 102:46134

ABSTRACT:  
(R) (RIO)P(O)CR<sub>2</sub>(OH)CHR<sub>3</sub>CR<sub>4</sub>R<sub>5</sub> (R, R<sub>1</sub> = alkyl, CH<sub>2</sub>Ph; R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>7</sub> = H, alkyl; R<sub>5</sub> = piperidinyl, X<sub>6</sub>, X<sub>7</sub>R<sub>8</sub>; R<sub>6</sub> = alkyl, alkanoyl, aryl; R<sub>8</sub> = alkyl, alkoxyalkyl; X = S, O) were prepared. Thus Me(CH<sub>2</sub>)<sub>4</sub>SH was treated with H<sub>2</sub>C=CHCHO and (EtO)<sub>2</sub>PH to give 80% Me(CH<sub>2</sub>)<sub>4</sub>CH<sub>2</sub>CH(OH)P(O)(OEt)<sub>2</sub> (I). At 56.0 kg/ha, postemergent, I gave complete control of Chenopodium album (lambsquarters).

SUPPL. TERM: hydroxy phosphonate herbicide prepn  
INDEX TERM: Herbicides  
(phosphonates,  $\alpha$ -hydroxy)  
INDEX TERM: 89222-47-9P 89222-48-0P 89222-49-1P 89222-50-4P  
89222-51-5P 89222-52-6P 89222-53-7P 89222-54-8P  
89222-55-9P 89222-56-0P 89222-57-1P 89222-59-3P  
89222-60-6P 94128-48-0P  
ROLE: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation and herbicidal activity of)

RX(25) RCT AB 111612-96-5  
RG RT AH 7693-26-7 KH, AJ 7447-41-8 LiCl  
PRO AT 111613-01-5, AU 111613-02-6  
SOL 67-68-5 DMSO, 109-99-9 THF

RX(26) OF 80 2 AD ==> AQ + AR



INDEX TERM: 89222-61-7P 89222-62-8P  
ROLE: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

INDEX TERM: 868-85-9  
ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with acrolein)

INDEX TERM: 762-04-9  
ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with acrolein and amines or mercaptans)

INDEX TERM: 60-24-2 74-85-1, reactions 75-33-2 75-64-9, reactions  
105-53-3 108-98-5, reactions 109-89-7, reactions  
110-66-7 110-89-4, reactions 111-92-2 594-39-8  
1639-09-4  
ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with acrolein and di-Et phosphite)

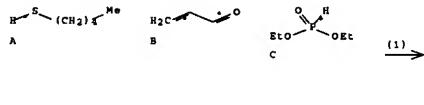
INDEX TERM: 17176-77-1  
ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with acrolein and diethylamine)

INDEX TERM: 107-03-9  
ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with carbonyl compds. and di-Et phosphite)

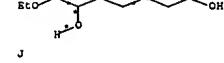
INDEX TERM: 107-02-8, reactions  
ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with mercaptans or amines and di-Et phosphite)

INDEX TERM: 78-85-3 78-94-4, reactions  
ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with propanethiol and di-Et phosphite)

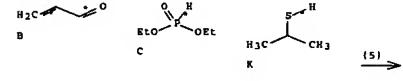
RX(1) OF 14 A + B + C ==&gt; D

RX(1) RCT A 110-66-7, B 107-02-8, C 762-04-9  
PRO D 89222-47-9

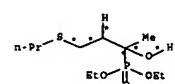
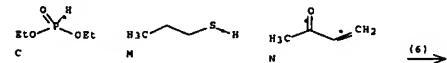
RX(2) OF 14 B + C + E ==&gt; F

RX(4) RCT B 107-02-8, C 762-04-9, I 60-24-2  
PRO J 89222-50-4

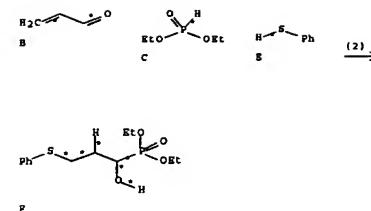
RX(5) OF 14 B + C + K ==&gt; L

RX(5) RCT B 107-02-8, C 762-04-9, K 75-33-2  
PRO L 89222-51-5

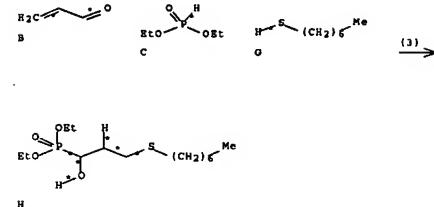
RX(6) OF 14 C + M + N ==&gt; O



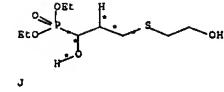
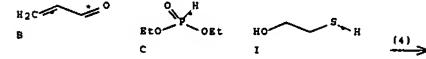
O

RX(2) RCT B 107-02-8, C 762-04-9, S 108-98-5  
PRO F 89222-48-0

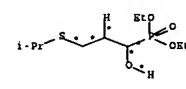
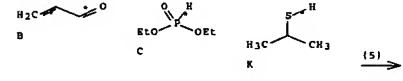
RX(3) OF 14 B + C + G ==&gt; H

RX(3) RCT B 107-02-8, C 762-04-9, G 1639-09-4  
PRO H 89222-49-1

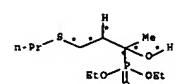
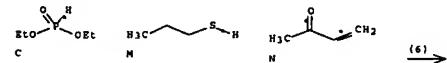
RX(4) OF 14 B + C + I ==&gt; J

RX(4) RCT B 107-02-8, C 762-04-9, I 60-24-2  
PRO J 89222-50-4

RX(5) OF 14 B + C + K ==&gt; L

RX(5) RCT B 107-02-8, C 762-04-9, K 75-33-2  
PRO L 89222-51-5

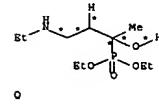
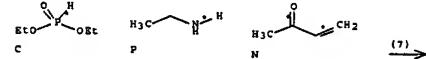
RX(6) OF 14 C + M + N ==&gt; O



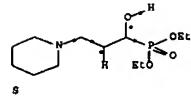
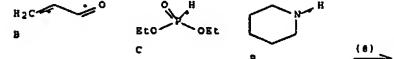
O

RX(6) RCT C 762-04-9, M 107-03-9, N 78-94-4  
PRO O 89222-53-7

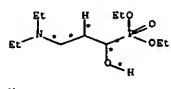
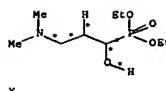
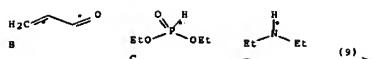
RX(7) OF 14 C + P + N ==&gt; Q

RX(7) RCT C 762-04-9, P 75-04-7, N 78-94-4  
PRO Q 89222-54-8

RX(8) OF 14 B + C + R ==&gt; S

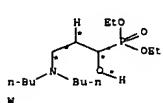
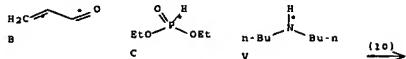
RX(8) RCT B 107-02-8, C 762-04-9, R 110-89-4  
PRO S 89222-55-9

RX(9) OF 14 B + C + T ==&gt; U



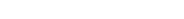
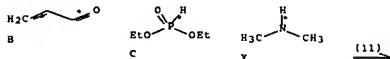
RX(9) RCT B 107-02-8, C 762-04-9, T 109-89-7  
PRO U 89222-56-0

RX(10) OF 14 B + C + V ==> W



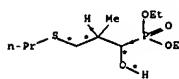
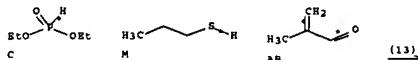
RX(10) RCT B 107-02-8, C 762-04-9, V 111-92-2  
PRO W 89222-59-3

RX(11) OF 14 B + C + X ==> Y



RX(12) RCT Z 67-56-1, B 107-02-8  
PRO AA 89222-62-8

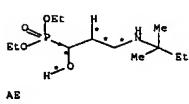
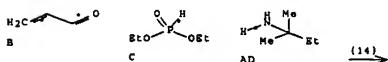
RX(13) OF 14 C + M + AB ==> AC



AC

RX(13) RCT C 762-04-9, M 107-03-9, AB 78-85-3  
PRO AC 89222-52-6

RX(14) OF 14 B + C + AD ==> AE



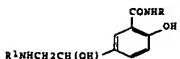
AE

RX(14) RCT B 107-02-8, C 762-04-9, AD 594-39-8  
PRO AB 89222-57-1

10/520362  
stereoisomers are described. The enantiomer with the (R) configuration at both asym. centers possessed most of the  $\beta$ -blocking activity but little  $\alpha$ -blocking activity. That with the (S) configuration at the alc. carbon and the (R) configuration on the amino substituent is predominantly an  $\alpha$ -adrenoceptor blocking agent.

SUPPL. TERM: salicylamide ethanamine deriv; labetalol stereoisomer  
INDEX TERM: prep antihypertensive  
Antihypertensives  
(labetalol enantiomers and related salicylamides as)  
INDEX TERM: Isomerism and Isomers  
(of labetalol, antihypertensive activity and)  
INDEX TERM: Molecular structure-biological activity relationship  
(antihypertensive of arylethanolamines derived from salicylamide)  
INDEX TERM: 24076-03-7 24076-19-5 81580-28-1  
ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(amidation of)  
INDEX TERM: 24085-18-5  
ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(amidation of, or condensation with acetophenone and formaldehyde)  
INDEX TERM: 68164-04-5  
ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(amidation reaction, with (bromoacetyl)salicylamide)  
INDEX TERM: 1611-38-7  
ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(catalytic hydrogenation of)  
INDEX TERM: 104-53-0  
ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(condensation of, (aminohydroxyethyl)salicylamide)  
INDEX TERM: 98-86-2, reactions  
ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(condensation of, with [(aminohydroxyethyl)amino]ethyl)s  
alicylate and formaldehyde)  
INDEX TERM: 32780-65-7  
ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(condensation of, with aldehydes and acetophenone)  
INDEX TERM: 103-79-7  
ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(condensation of, with aminoacetophenone derivative)  
INDEX TERM: 78-95-5  
ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(condensation of, with aniline derivative)  
INDEX TERM: 2627-86-3 3886-69-9  
ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(condensation of, with benzylacetone)  
INDEX TERM: 73866-23-6  
ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(condensation of, with benzylamine derivative, and amidation  
of)  
INDEX TERM: 2550-26-7  
ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(condensation of, with  $\alpha$ -methylbenzylamine)  
INDEX TERM: 75659-08-4P 81602-13-3P 81602-14-4P 81602-15-5P  
ROLE: BAC (Biological activity or effector, except adverse);  
BSU (Biological study, unclassified); SPN (Synthetic  
preparation); THU (Therapeutic use); BIOL (Biological  
study); PREP (Preparation); USES (Uses)

L27 ANSWER 7 OF 8 CASREACT COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 96:199236 CASREACT Full-text  
TITLE: Arylethanolamines derived from salicylamide with  $\alpha$ - and  $\beta$ -adrenoceptor blocking activities. Preparation of labetalol, its enantiomers and related salicylamides  
AUTHOR(S): Clifton, James E.; Collins, Ian; Hallett, Peter; Hartley, David; Lupton, Lawrence H. C.; Wickes, Philip D.  
CORPORATE SOURCE: Chem. Dep., Glaxo Group Res. Ltd., Ware/Herts., SG12 6DJ, UK  
SOURCE: Journal of Medicinal Chemistry (1982), 25(6), 670-9  
CODEN: JMCMAR; ISSN: 0022-2623  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
CLASSIFICATION: 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
GRAPHIC IMAGE:



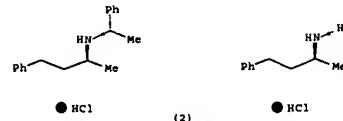
ABSTRACT:  
Phenylethanolamines I (R = H, Me, PhCH<sub>2</sub>, HOCH<sub>2</sub>CH<sub>2</sub>, NH<sub>2</sub>; R<sub>1</sub> = alkyl or substituted alkyl) were prepared and shown to possess  $\beta$ -adrenergic blocking properties. When the basic N atom was substituted by some aralkyl groups, the compds. also blocked  $\alpha$ -adrenoceptors. Labetalol (I; R = H, R<sub>1</sub> = PhCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Me) is antihypertensive in animals and man, and syntheses of its 4

INDEX TERM: (preparation and antihypertensive activity of)  
 INDEX TERM: 32780-63-5P 36256-61-8P  
 ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent); (preparation and catalytic hydrogenation of)  
 INDEX TERM: 80744-23-6P 81580-35-0P  
 ROLE: SPN (Synthetic preparation); PREP (Preparation); (preparation and condensation with (bromoacetyl)salicylamide)  
 INDEX TERM: 81580-36-1P 81580-38-3P  
 ROLE: RCT (Reactant); SPN (Synthetic preparation); PRSP (Preparation); RACT (Reactant or reagent); (preparation and hydrogenation-benzylation of)  
 INDEX TERM: 24076-04-8P 24076-14-0P 75615-55-3P 75615-56-4P  
 61580-32-7P 81580-33-8P 81580-37-2P 81585-06-0P  
 ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent); (preparation and hydrogenolysis of)  
 INDEX TERM: 72487-35-5P  
 ROLE: SPN (Synthetic preparation); PREP (Preparation); (preparation and resolution of racemic)  
 INDEX TERM: 826-16-4P  
 ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent); (preparation and N-benzylation of)  
 INDEX TERM: 24076-05-9P 24076-10-6P 24076-11-7P 24076-12-8P  
 24076-13-9P 24076-15-1P 24076-21-9P 24084-97-7P  
 25034-32-6P 32780-35-1P 32780-39-5P 32780-69-1P  
 32780-70-4P 32780-71-5P 32780-72-6P 32780-73-7P  
 36256-60-7P 36270-45-8P 54646-15-0P 56290-92-7P  
 63416-60-4P 63416-61-5P 63416-66-0P 64449-93-0P  
 64450-21-1P 64450-22-2P 64779-91-5P 64779-92-6P  
 64779-93-7P 70161-10-3P 72371-11-0P 75659-07-3P  
 81579-44-4P 81579-45-5P 81579-46-6P 81579-47-7P  
 81579-48-8P 81579-49-9P 81579-50-2P 81579-51-3P  
 81579-52-4P 81579-54-6P 81579-55-7P 81579-56-8P  
 81579-57-9P 81579-58-0P 81579-59-1P 81579-60-4P  
 81580-04-3P 81580-05-4P 81580-06-5P 81580-07-6P  
 81580-08-7P 81580-09-8P 81580-10-1P 81580-11-2P  
 81580-12-3P 81580-13-4P 81580-14-5P 81580-15-6P  
 81580-16-7P 81580-17-8P 81580-18-9P 81580-19-0P  
 81580-20-3P 81580-21-4P 81580-22-5P 81580-23-6P  
 81580-24-7P 81580-25-8P 81580-26-9P 81580-27-0P  
 81580-29-2P 81580-30-5P 81580-31-6P 81580-34-9P  
 ROLE: SPN (Synthetic preparation); PREP (Preparation); (preparation of)  
 INDEX TERM: 72487-34-4P  
 ROLE: SPN (Synthetic preparation); PREP (Preparation); (preparation of enantiomeric components of racemic)  
 INDEX TERM: 459-59-6  
 ROLE: RCT (Reactant); RACT (Reactant or reagent); (reaction of, with chloropropane)  
 INDEX TERM: 30566-92-8  
 ROLE: RCT (Reactant); RACT (Reactant or reagent); (reaction of, with phenylpropanone)

RX(1) OF 182 ...A ==&gt; B...

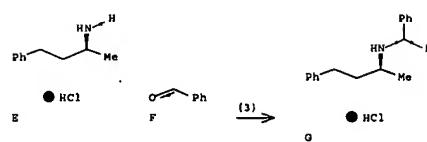
RX(1) RCT A 81580-32-7  
 PRO B 826-16-4  
 CAT 144-55-8 NaHCO<sub>3</sub>

RX(2) OF 182 ...D ==&gt; E...



RX(2) RCT D 81580-33-8  
 PRO E 81580-34-9  
 CAT 144-55-8 NaHCO<sub>3</sub>

RX(3) OF 182 ...E + F ==&gt; G...

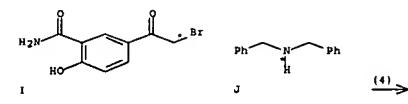


RX(3) RCT E 81580-34-9, F 100-52-7  
 RGT H 7647-01-0 HCl  
 PRO G 80744-23-6  
 CAT 144-55-8 NaHCO<sub>3</sub>

81

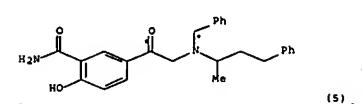
82

RX(4) OF 182 I + J ==&gt; K...



YIELD 53%  
 RX(4) RCT I 73866-23-6, J 103-49-1  
 PRO K 30566-92-8

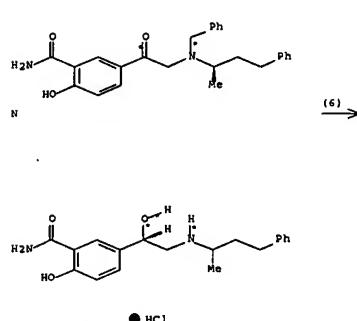
RX(5) OF 182 ...L ==&gt; M



YIELD 67%  
 M

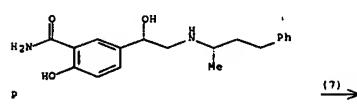
RX(5) RCT L 81579-50-2  
 RGT H 7647-01-0 HCl  
 PRO M 32780-64-6

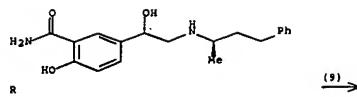
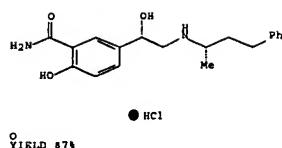
RX(6) OF 182 ...N ==&gt; O.



RX(6) RCT N 81580-36-1  
 PRO O 72487-34-4

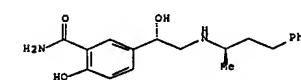
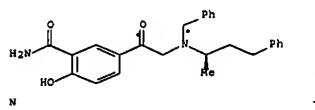
RX(7) OF 182 ...P ==&gt; Q





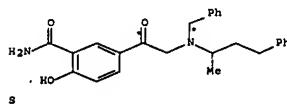
RX(7) RCT P 72487-32-2  
RGT H 7647-01-0 HCl  
PRO O 72487-34-4

RX(8) OF 182 ...N ===> Q



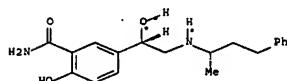
RX(9) RCT R 72487-31-1  
RGT H 7647-01-0 HCl  
PRO Q 72487-35-5

RX(10) OF 182 ...S ===> O



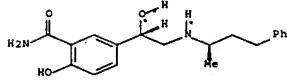
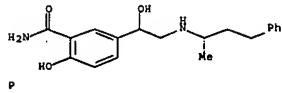
RX(8) RCT N 81580-36-1  
PRO Q 72487-35-5

RX(9) OF 182 ...R ===> Q



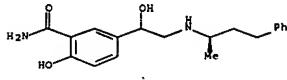
RX(10) RCT S 81580-38-3  
PRO O 72487-34-4

RX(11) OF 182 P ===> O



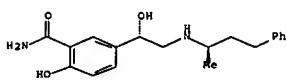
RX(12) RCT S 81580-38-3  
PRO O 72487-35-5

RX(13) OF 182 R ===> O



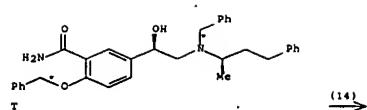
RX(11) RCT P 72487-32-2  
RGT H 7647-01-0 HCl  
PRO O 72487-34-4

RX(12) OF 182 ...S ===> Q



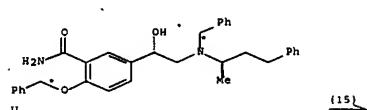
RX(13) RCT R 72487-31-1  
RGT H 7647-01-0 HCl  
PRO Q 72487-35-5

RX(14) OF 182 T ===> P...



RX(14) RCT T 75615-55-3  
PRO P 72487-32-2

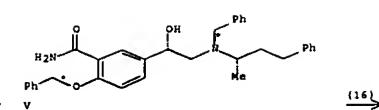
RX(15) OF 182 U ==> R...



RX(15) RCT U 81580-37-2  
PRO R 72487-31-1

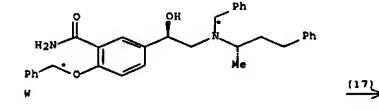
RX(16) OF 182 V ==> P...

89



RX(16) RCT V 81585-06-0  
PRO P 72487-32-2

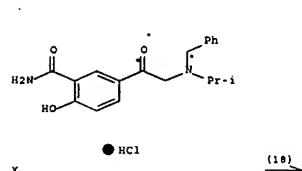
RX(17) OF 182 W ==> R...



RX(17) RCT W 75615-56-4  
PRO R 72487-31-1

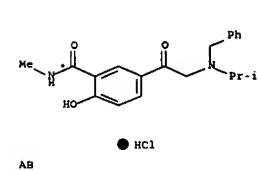
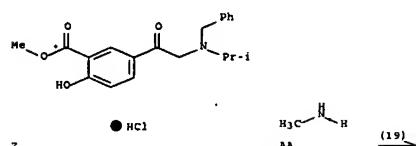
RX(18) OF 182 ...X ==> Y

90



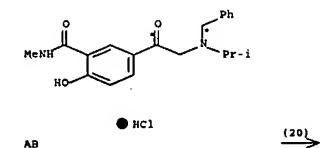
RX(18) RCT X 24076-04-8  
PRO Y 24076-05-9

RX(19) OF 182 Z + AA ==> AB...



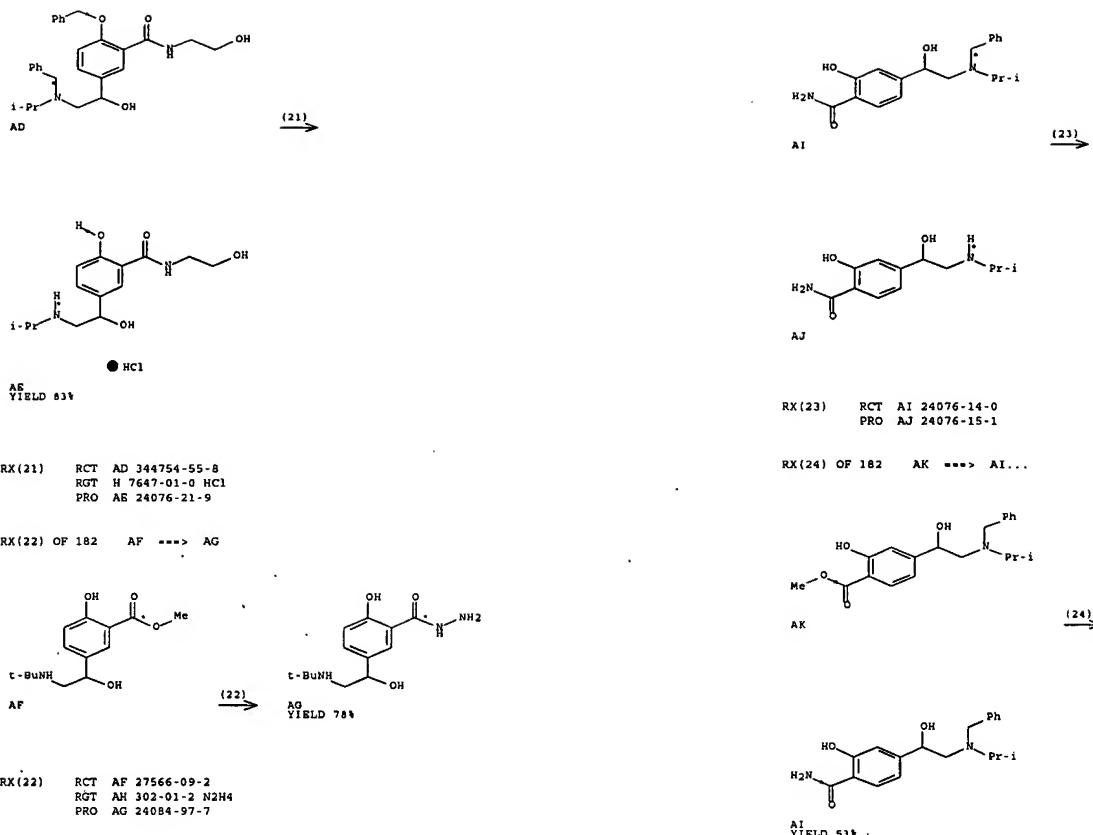
RX(19) RCT Z 24076-03-7, AA 74-89-5  
PRO AB 24076-12-8

RX(20) OF 182 ...AB ==> AC



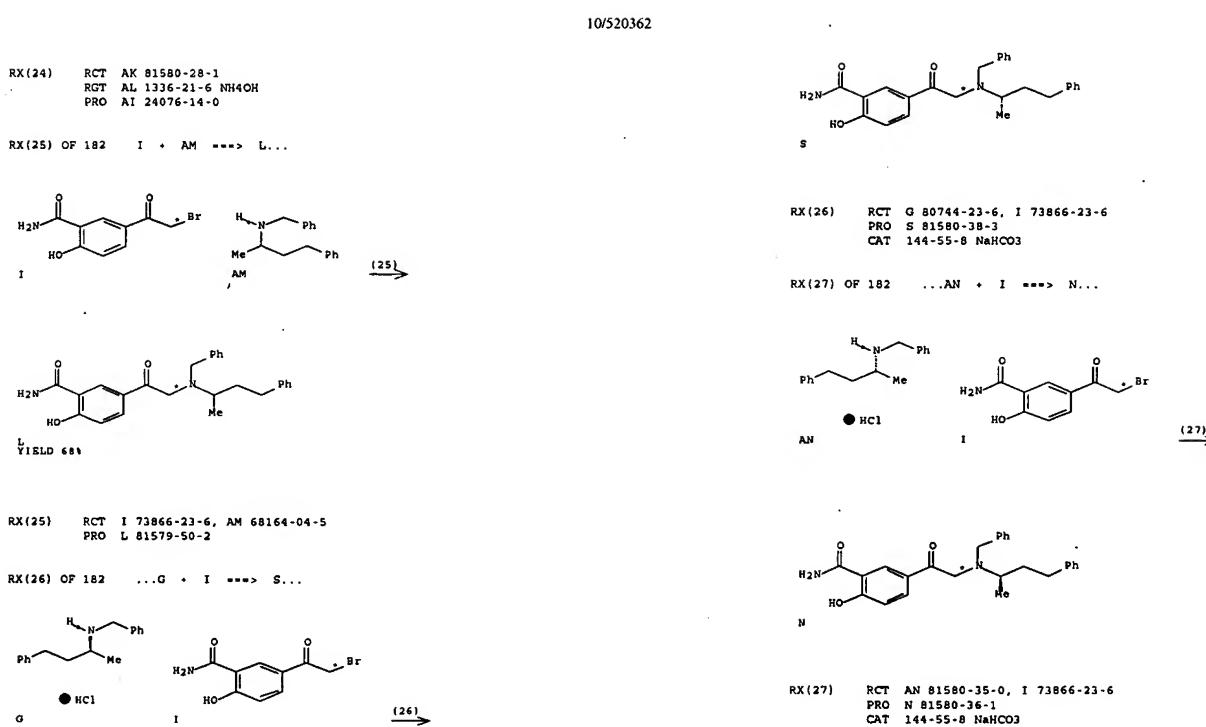
RX(20) RCT AB 24076-12-8  
PRO AC 24076-13-9

RX(21) OF 182 ...AD ==> AB



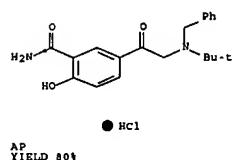
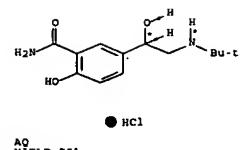
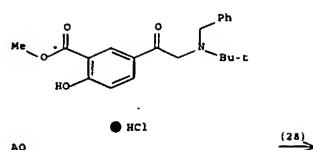
93

94



95

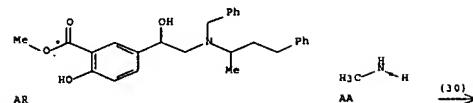
96



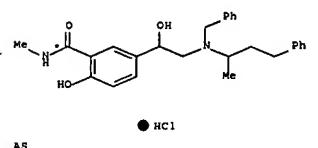
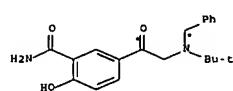
RX(28) RCT AP 36270-45-8

PRO AQ 24076-10-6

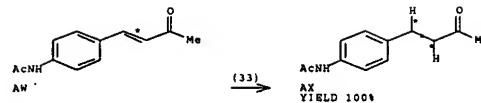
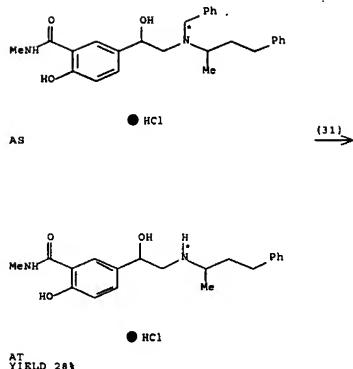
RX(29) OF 182 AR + AA ==&gt; AS...

RX(28) RCT AO 27475-26-9  
RCT AL 1316-21-6 NH4OH  
PRO AP 36270-45-8

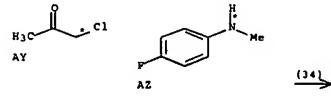
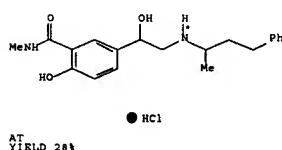
RX(29) OF 182 ...AP ==&gt; AQ

RX(30) RCT AR 345948-53-0, AA 74-89-5  
PRO AS 81579-51-3

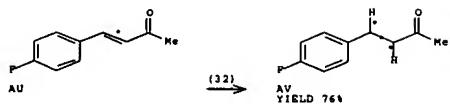
RX(31) OF 182 ...AS ==&gt; AT

RX(31) RCT AS 81579-51-3  
PRO AT 81580-27-0

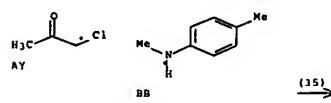
RX(32) OF 182 AU ==&gt; AV...

RX(31) RCT AS 81579-51-3  
PRO AT 81580-27-0

RX(32) OF 182 AU ==&gt; AV...

RX(34) RCT AV 78-95-5, AZ 459-59-6  
PRO BA 64450-21-1  
CAT 144-55-8 NaHCO3

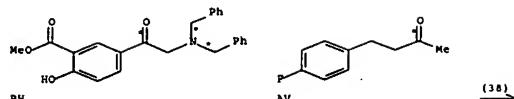
RX(35) OF 182 AV + BB ==&gt; BC...

RX(32) RCT AU 1611-38-7  
PRO AV 63416-61-5

RX(33) OF 182 AV ==&gt; AX...

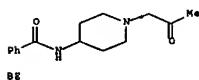
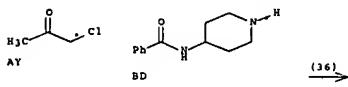
PRO BG B1580-31-6  
CAT 144-55-8 NaHCO<sub>3</sub>

RX(38) OF 182 ...BH + AV ==&gt; BI...



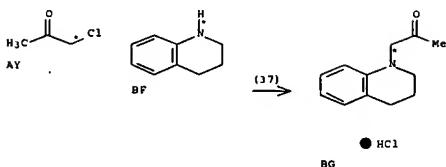
RX(35) RCT AV 78-95-5, BB 623-08-5  
PRO BC 64450-22-2  
CAT 144-55-8 NaHCO<sub>3</sub>

RX(36) OF 182 AY + BD ==&gt; BE...



RX(36) RCT AY 78-95-5, BD 33953-37-6  
PRO BB 81580-30-5  
CAT 144-55-8 NaHCO<sub>3</sub>

RX(37) OF 182 AY + BF ==&gt; BG...



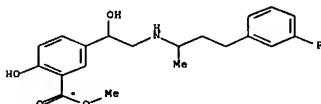
RX(37) RCT AY 78-95-5, BF 635-46-1

101

102

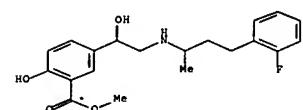
RX(40) RCT BL 63416-66-0  
RGT AL 1336-21-6 NH<sub>4</sub>OH  
PRO BM 64779-92-6

RX(41) OF 182 BN ==&gt; BO



RX(39) RCT BH 36270-04-9, BJ 55418-52-5  
RGT H 7647-01-0 HCl  
PRO BK 56290-92-7

RX(40) OF 182 ...BL ==&gt; BM

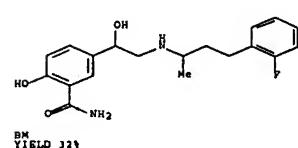


BL

→

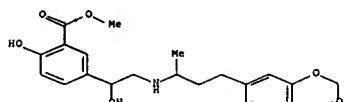
RX(41) RCT BN 63416-63-7  
RGT AL 1336-21-6 NH<sub>4</sub>OH  
PRO BO 81580-09-8

RX(42) OF 182 ...BK ==&gt; BP



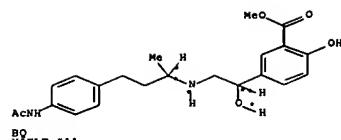
BK

YIELD 32%

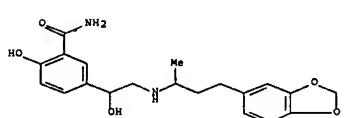


BK

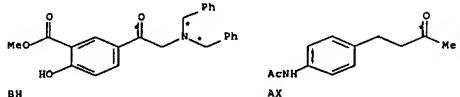
(42)



YIELD 51%

BP  
YIELD 81%RX(42) RCT BK 56290-92-7  
RGT H 7647-01-0 HCl, AL 1336-21-6 NH4OH  
PRO BP 70161-10-3

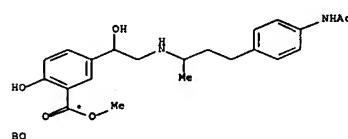
RX(43) OF 182 ...BH + AX ==&gt; BQ...



(43)

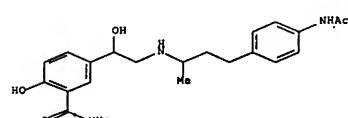
RX(43) RCT BH 36270-04-9, AX 54646-15-0  
PRO BQ 81579-44-4

RX(44) OF 182 ...BQ ==&gt; BR



BQ

(44)



● HCl

YIELD 94%

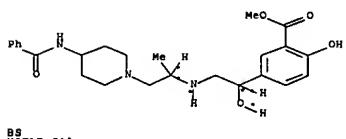
RX(44) RCT BQ 81579-44-4  
RGT H 7647-01-0 HCl, AL 1336-21-6 NH4OH  
PRO BR 81580-14-5

RX(45) OF 182 ...BE + BH ==&gt; BS...

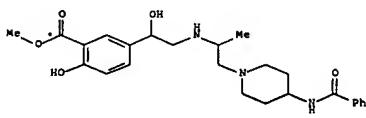
105

106

(45)

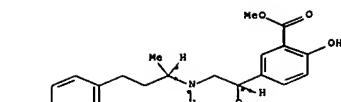
BS  
YIELD 51%RX(45) RCT BS 81580-30-5, BH 36270-04-9  
PRO BS 81579-48-8

RX(46) OF 182 ...BS ==&gt; BT



BS

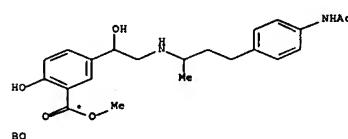
(46)



YIELD 51%

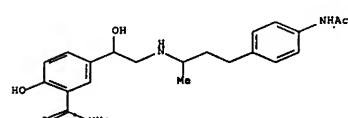
RX(43) RCT BH 36270-04-9, AX 54646-15-0  
PRO BQ 81579-44-4

RX(44) OF 182 ...BQ ==&gt; BR



BQ

(44)



● HCl

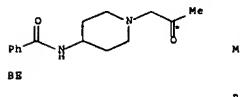
YIELD 94%

RX(44) RCT BQ 81579-44-4  
RGT H 7647-01-0 HCl, AL 1336-21-6 NH4OH  
PRO BR 81580-14-5

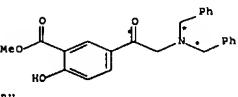
RX(45) OF 182 ...BE + BH ==&gt; BS...

105

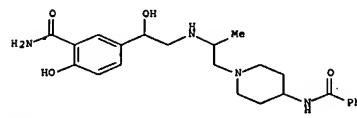
106



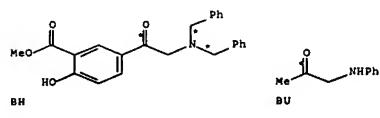
BS



BH

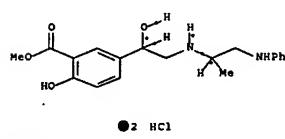
BT  
YIELD 86%RX(46) RCT BS 81579-48-8  
RGT AL 1336-21-6 NH4OH  
PRO BT 81579-57-9

RX(47) OF 182 BH + BU ==&gt; BV...



BU

(47)



● 2 HCl

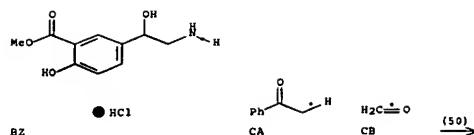
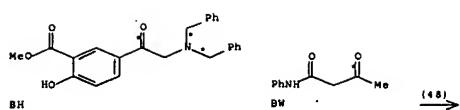
YIELD 84%

RX(47) RCT BH 36270-04-9, BU 4504-29-4  
RGT H 7647-01-0 HCl  
PRO BV 81579-49-9

RX(48) OF 182 BH + BW ==&gt; BX...

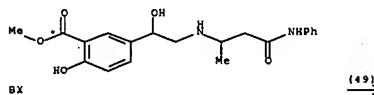
107

108



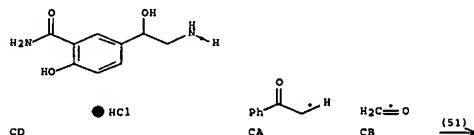
RX(48)    RCT BH 36270-04-9, BW 102-01-2  
PRO BX 64449-93-0

RX(49) OF 182    ...BX     $\xrightarrow{(48)}$  BY



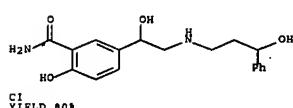
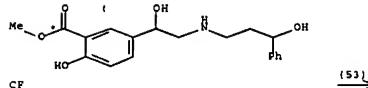
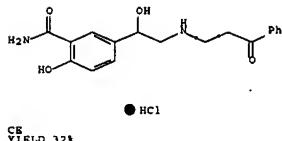
RX(50)    RCT BZ 24085-18-5, CA 98-86-2, CB 50-00-0  
PRO CC 81579-45-5

RX(51) OF 182    ...CD + CA + CB     $\xrightarrow{(50)}$  CC



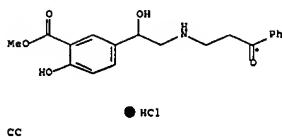
RX(49)    RCT BX 64449-93-0  
RGT AL 1336-21-6 NH4OH  
PRO BY 81580-25-8

RX(50) OF 182    BZ + CA + CB     $\xrightarrow{(50)}$  CC...



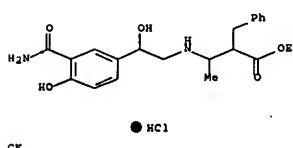
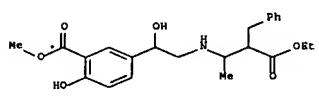
RX(51)    RCT CD 32780-65-7, CA 98-86-2, CB 50-00-0  
PRO CC 81580-18-9

RX(52) OF 182    ...CC     $\xrightarrow{(51)}$  CF...



RX(53)    RCT CF 81579-46-6  
RGT AL 1336-21-6 NH4OH  
PRO CI 81579-59-1

RX(54) OF 182    CJ     $\xrightarrow{(53)}$  CK

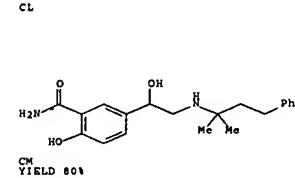
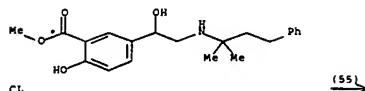


RX(52)    RCT CC 81579-45-5  
RGT CJ 16949-15-8 LiBH<sub>4</sub>  
PRO CF 81579-46-6  
CAT 16940-66-2 NaBH<sub>4</sub>

RX(53) OF 182    ...CF     $\xrightarrow{(52)}$  CJ

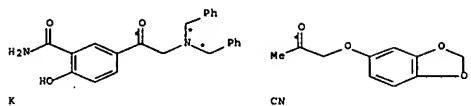
RX(54) RCT CJ 81579-47-7  
RGT AL 1336-21-6 NH4OH  
PRO CK 81579-58-0

RX(55) OF 182 CL ===> CM



RX(55) RCT CL 345651-86-7  
RGT AL 1336-21-6 NH4OH  
PRO CM 32780-39-5

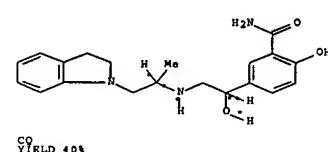
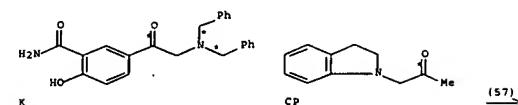
RX(56) OF 182 ...K + CN ===> CO



(56) →

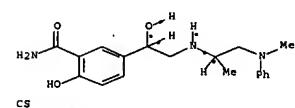
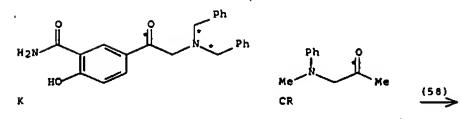
RX(56) RCT K 30566-92-8, CN 99807-06-4  
PRO CO 81580-20-3

RX(57) OF 182 ...K + CP ===> CO



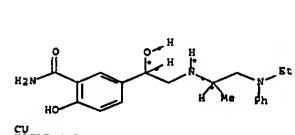
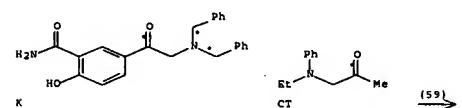
RX(57) RCT K 30566-92-8, CP 344304-70-7  
PRO CO 81579-55-7

RX(58) OF 182 ...K + CR ===> CS



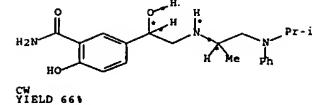
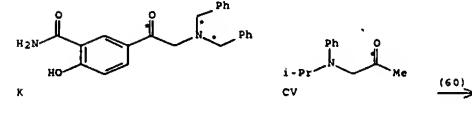
RX(58) RCT K 30566-92-8, CR 15885-06-0  
PRO CS 72371-11-0

RX(59) OF 182 ...K + CT ===> CU



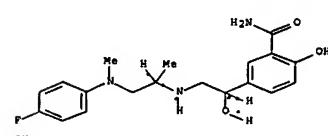
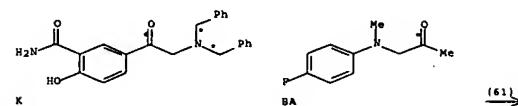
RX(59) RCT K 30566-92-8, CT 31399-19-6  
PRO CU 81580-04-3

RX(60) OF 182 ...K + CV ===> CW



RX(60) RCT K 30566-92-8, CV 344308-74-3  
PRO CW 81580-05-4

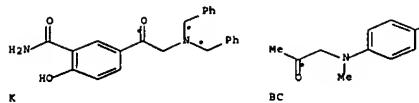
RX(61) OF 182 ...K + BA ===> CX



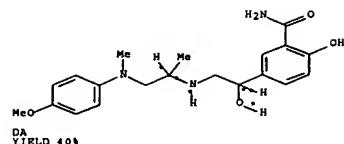
RX(61) RCT K 30566-92-8, BA 64450-21-1

PRO CX 81580-22-5

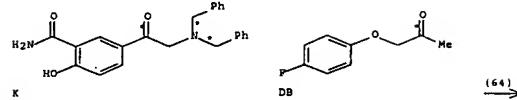
RX(62) OF 182 ...K + BC ===&gt; CY



(62) →

RX(63) RCT K 30566-92-8, CZ 64450-19-7  
PRO DA 81580-24-7

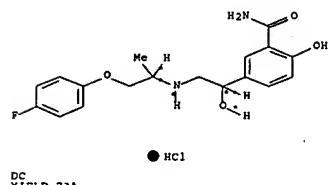
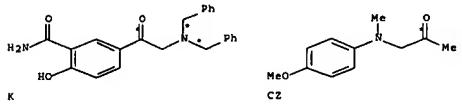
RX(64) OF 182 ...K + DB ===&gt; DC



(64) →

RX(62) RCT K 30566-92-8, BC 64450-22-2  
PRO CY 81580-21-4

RX(63) OF 182 ...K + CZ ===&gt; DA

RX(64) RCT K 30566-92-8, DB 81580-29-2  
RGT H 7647-01-0 HCl  
PRO DC 81580-19-0

RX(65) OF 182 ...K + DD ===&gt; DE

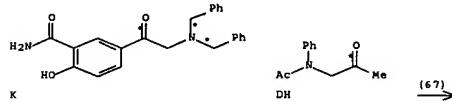
(63) →

117

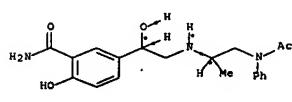
118

RX(66) RCT K 30566-92-8, DF 5409-60-9  
RGT H 7647-01-0 HCl  
PRO DG 32780-35-1

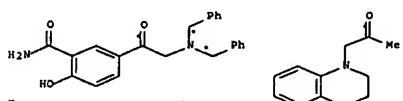
RX(67) OF 182 ...K + DH ===&gt; DI



(67) →

RX(67) RCT K 30566-92-8, DH 64450-18-6  
RGT H 7647-01-0 HCl  
PRO DI 81580-06-5

RX(68) OF 182 ...K + BG ===&gt; DJ

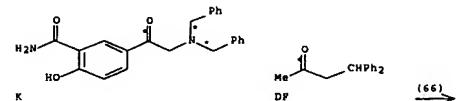


(68) →

● HCl

RX(65) RCT K 30566-92-8, DD 103-79-7  
RGT H 7647-01-0 HCl  
PRO DB 81579-52-4

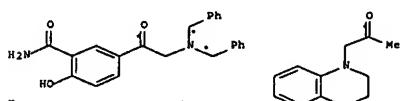
RX(66) OF 182 ...K + DF ===&gt; DG



(66) →

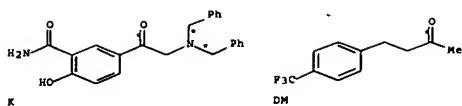
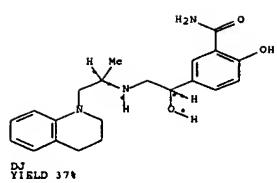
RX(67) RCT K 30566-92-8, DH 64450-18-6  
RGT H 7647-01-0 HCl  
PRO DI 81580-06-5

RX(68) OF 182 ...K + BG ===&gt; DJ

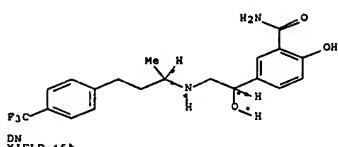


(68) →

● HCl  
YIELD 27%



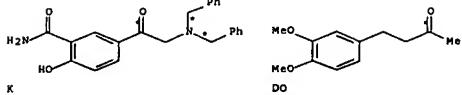
(70) →

RX(68) RCT K 30566-92-8, BG 81580-31-6  
PRO DJ 81579-56-8

RX(69) OF 182 ...K + K ==&gt; DL



(69) →

RX(70) RCT K 30566-92-8, DM 57132-19-1  
PRO DN 81580-08-7

RX(71) OF 182 ...K + DO ==&gt; DP

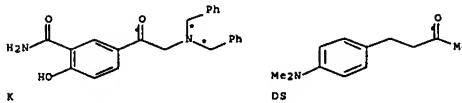


(71) →

RX(69) RCT DK 7774-79-0, K 30566-92-8  
PRO DL 81580-07-6

RX(70) OF 182 ...K + DM ==&gt; DN

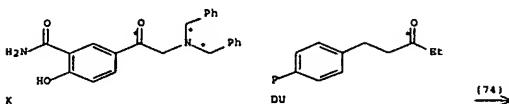
RX(73) OF 182 ...K + DS ==&gt; DT



(71) →

RX(73) RCT K 30566-92-8, DS 30780-30-4  
PRO DT 81580-13-4

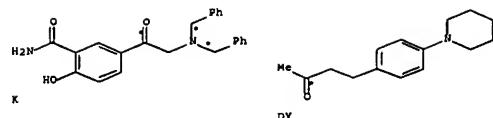
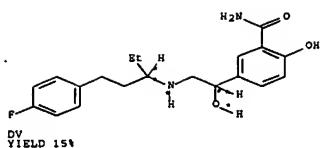
RX(74) OF 182 ...K + DU ==&gt; DV



(74) →

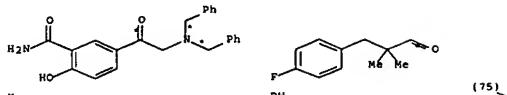
DR YIELD 90%

RX(72) RCT K 30566-92-8, DO 74248-99-0  
PRO DR 81580-11-2

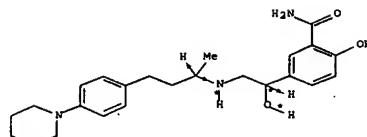


RX(74) RCT K 30566-92-8, DU 63416-75-1  
PRO DV 81580-16-7

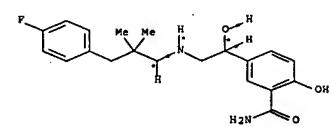
RX(75) OF 182 ...K + DW ==> DX



(75) →



● 2 HCl  
DZ YIELD 27%

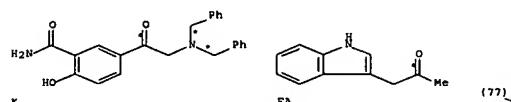


RX(75) RCT K 30566-92-8, DW 4092-92-6  
RGT H 7647-01-0 HCl  
PRO DX 81580-17-8

RX(76) OF 182 ...K + DY ==> DZ

RX(76) RCT K 30566-92-8, DY 344304-03-6  
RGT H 7647-01-0 HCl  
PRO DZ 81580-15-6

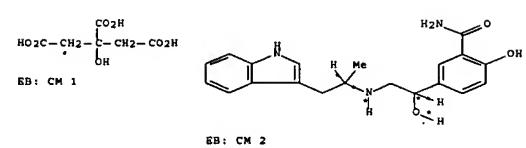
RX(77) OF 182 ...K + EA ==> EB



(77) →

125

126

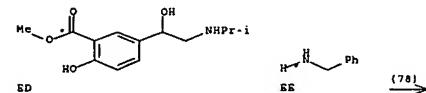


10/520362

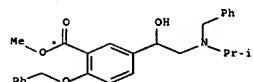
10/520362

RX(77) RCT K 30566-92-8, EA 1201-26-9  
PRO EB 81579-54-6  
CAT 77-92-9 Citric acid

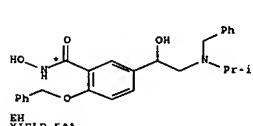
RX(78) OF 182 ED + EB ==> EF



(78) →



● HCl  
EG



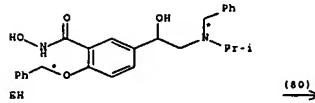
RX(78) RCT ED 36270-12-9, EB 100-46-9  
PRO EF 24076-11-7

RX(79) OF 182 EG ==> EH...

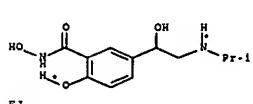
RX(79) RCT ED 36270-12-9, EB 100-46-9  
PRO EF 24076-11-7

RX(79) RCT EG 24076-19-5  
RGT EI 7803-49-8 NH2OH  
PRO EH 36256-61-8

RX(80) OF 182 ...EH ==> EJ



(80) →



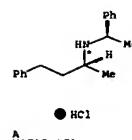
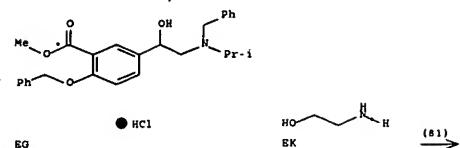
RX(80) RCT EH 36256-61-8

127

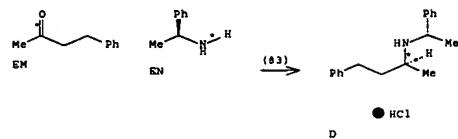
128

PRO BJ 36256-60-7

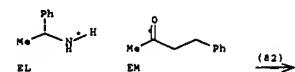
RX(81) OF 182 EG + EK ==&gt; AD...

RX(82) RCT EL 3886-69-9, EM 2550-26-7  
RGT H 7647-01-0 HCl  
PRO A 81580-32-7

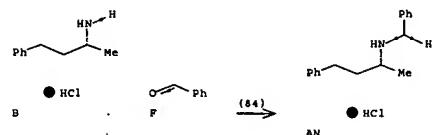
RX(83) OF 182 EM + EN ==&gt; D...

RX(81) RCT EG 24076-19-5, EK 141-43-5  
PRO AD 344754-55-8

RX(82) OF 182 EL + EM ==&gt; A...

RX(83) RCT EM 2550-26-7, EN 2627-86-3  
RGT H 7647-01-0 HCl  
PRO D 81580-33-8

RX(84) OF 182 ...B + F ==&gt; AN...

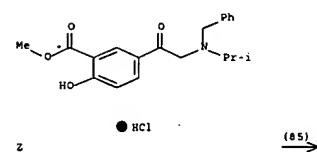
RX(84) RCT B 826-16-4, F 100-52-7  
RGT H 7647-01-0 HCl

129

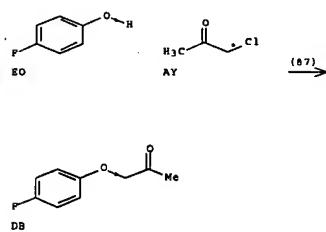
130

PRO AN 81580-35-0  
CAT 144-55-8 NaHCO3

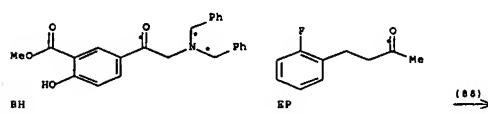
RX(85) OF 182 Z ==&gt; X...

RX(86) RCT BZ 24085-18-5  
RGT AL 1336-21-6 NH4OH  
PRO CD 32780-65-7

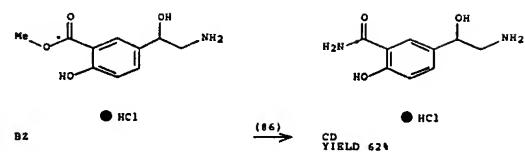
RX(87) OF 182 EO + AY ==&gt; DB...

RX(87) RCT EO 371-41-5, AY 78-95-5  
PRO DB 81580-29-2  
CAT 144-55-8 NaHCO3

RX(88) OF 182 BH + BP ==&gt; BL...

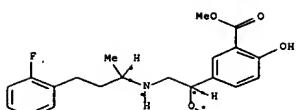
RX(85) RCT Z 24076-03-7  
RGT AL 1336-21-6 NH4OH  
PRO X 24076-04-8

RX(86) OF 182 BZ ==&gt; CD...



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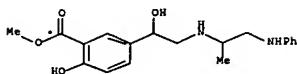
132



● HCl  
BL YIELD 76%

RX(89) RCT BI 63416-60-4  
RGT H 7647-01-0 HCl, AL 1336-21-6 NH4OH  
PRO EQ 64779-91-5

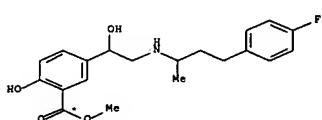
RX(90) OF 182 ...BV ==> SR



● 2 HCl  
BV (90) ==>

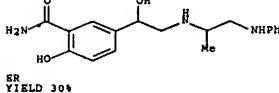
RX(88) RCT BH 36270-04-9, EP 63416-65-9  
RGT H 7647-01-0 HCl  
PRO BL 63416-66-0

RX(89) OF 182 ...BI ==> EQ



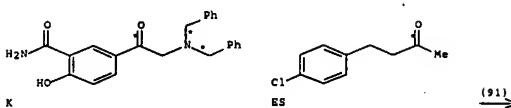
● HCl (89) ==>

BI



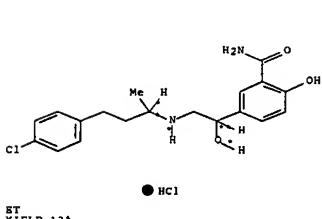
RX(90) RCT BV 81579-49-9  
RGT AL 1336-21-6 NH4OH  
PRO ER 81579-60-4

RX(91) OF 182 ...K + ES ==> ET



K ES (91) ==>

● HCl  
EQ YIELD 90%



ET YIELD 13%

L27 ANSWER 8 OF 8 CASREACT COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 95:61370 CASREACT Full-text  
TITLE: Synthesis of substituted 3-amino alcohols by reduction  
of oximes of  $\beta$ -keto alcohols  
AUTHOR(S): Latypova, F. N.; Malina, Yu. F.; Unkovskii, B. V.  
CORPORATE SOURCE: USSR  
SOURCE: Khimiya i Tekhnologiya Organicheskikh Proizvodstv  
(1979), 9(2), 3-8  
CODEN: KTOPDN  
DOCUMENT TYPE: Journal  
LANGUAGE: Russian  
CLASSIFICATION: 23-7 (Aliphatic Compounds)  
Section cross-reference(s): 25

ABSTRACT: Condensation reaction of HCHO with PhCOEt and MeOH containing KOH yielded 80% HOCH<sub>2</sub>CHMeCOOPh (1). Oximation of HOCCR<sub>1</sub>CHR<sub>2</sub>CO<sub>2</sub>R<sub>3</sub> (R = R<sub>1</sub> = R<sub>3</sub> = Me, R<sub>2</sub> = H; R = R<sub>1</sub> = H, R<sub>2</sub> = R<sub>3</sub> = Me; R = H, R<sub>1</sub> = R<sub>2</sub> = R<sub>3</sub> = Me) and 1 gave 65-85% yield of the corresponding HOCCR<sub>1</sub>CHR<sub>2</sub>R<sub>3</sub>:NOH, which were reduced with Raney Ni and with LiAlH<sub>4</sub> to give 50-70% and 35-50% HOCCR<sub>1</sub>CHR<sub>2</sub>CH<sub>3</sub>NH<sub>2</sub> (same R-R<sub>3</sub>), resp.

SUPPL. TERM: amino alc; oxime hydroxy ketone redn  
INDEX TERM: Oximes

ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(of  $\beta$ -hydroxy ketones, preparation and reduction of,  
 $\beta$ -amino alc. by)

INDEX TERM: Ketones, reactions

ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(oximation of)

INDEX TERM: Alcohols, preparation

ROLE: SPN (Synthetic preparation); PREP (Preparation)  
(amino,  $\beta$ -, preparation of, by reduction of oximes of  
 $\beta$ -hydroxy ketones)

INDEX TERM: 93-55-0

ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(condensation reaction of, with formaldehyde)

INDEX TERM: 50-00-0, reactions

ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(condensation reaction of, with propiophenone)

INDEX TERM: 123-42-2 565-79-7 3393-64-4

ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(oximation of)

INDEX TERM: 16735-22-1P

ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP  
(Preparation); RACT (Reactant or reagent)  
(preparation and oximation of)

INDEX TERM: 17918-67-1P 69125-01-5P 78401-96-4P 78401-97-5P

ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP  
(Preparation); RACT (Reactant or reagent)  
(preparation and reduction of,  $\beta$ -amino alc. by)

INDEX TERM: 70772-78-0P 78401-94-2P 78401-95-3P 78420-43-6P

ROLE: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RX(92) RCT DR 81580-11-2

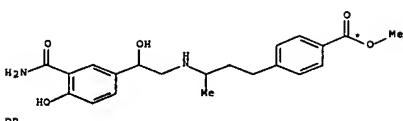
RGT H 7647-01-0 HCl, AL 1336-21-6 NH4OH

PRO EU 81580-12-3

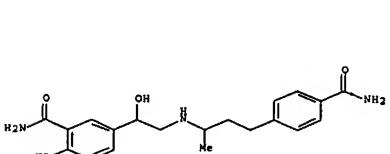
RX(1) OF 66 A + B ==> C...

RX(91) RCT K 30566-92-8, ES 3506-75-0  
RGT H 7647-01-0 HCl  
PRO ET 64779-93-7

RX(92) OF 182 ...DR ==> EU



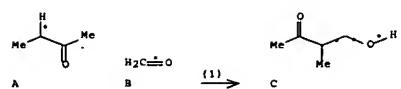
(92) ==>



● HCl

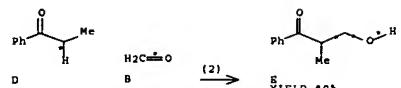
EU YIELD 41%

RX(92) RCT DR 81580-11-2  
RGT H 7647-01-0 HCl, AL 1336-21-6 NH4OH  
PRO EU 81580-12-3



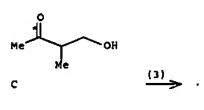
RX(1) RCT A 78-93-3, B 50-00-0  
PRO C 3393-64-4

RX(2) OF 66 D + B ==> E...



RX(2) RCT D 93-55-0, B 50-00-0  
PRO E 16735-22-1

RX(3) OF 66 ...C ==> F...



F  
YIELD 85%

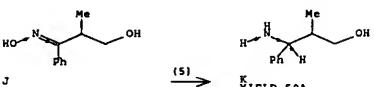
RX(3) RCT C 3393-64-4  
RGD G 7803-49-8 NH2OH  
PRO F 69125-01-5

RX(4) OF 66 H ==> I...



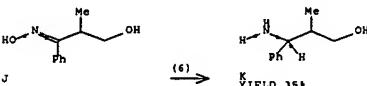
RX(4) RCT H 123-42-2  
RGD G 7803-49-8 NH2OH  
PRO I 17918-67-1

RX(5) OF 66 ...J ==> K



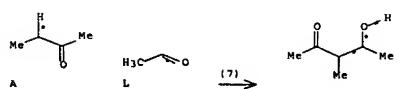
RX(5) RCT J 78401-97-5  
PRO K 78401-95-3

RX(6) OF 66 J ==> K



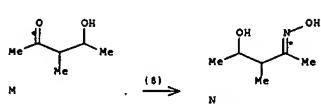
RX(6) RCT J 78401-97-5  
PRO K 78401-95-3

RX(7) OF 66 A + L ==> M...



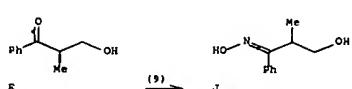
RX(7) RCT A 78-93-3, L 75-07-0  
PRO M 565-79-7

RX(8) OF 66 ...M ==> N...



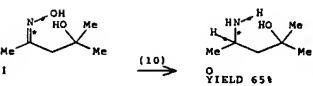
RX(8) RCT M 565-79-7  
RGD G 7803-49-8 NH2OH  
PRO N 78401-96-4

RX(9) OF 66 ...B ==> J...



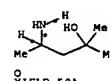
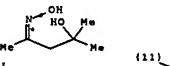
RX(9) RCT B 16735-22-1  
RGD G 7803-49-8 NH2OH  
PRO J 78401-97-5

RX(10) OF 66 ...I ==> O



RX(10) RCT I 17918-67-1  
PRO O 70772-78-0

RX(11) OF 66 I ==> O



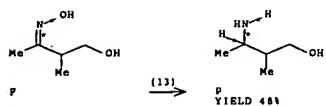
RX(11) RCT I 17918-67-1  
PRO O 70772-78-0

RX(12) OF 66 ...F ==> P



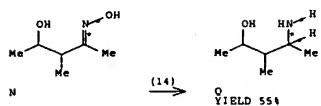
RX(12) RCT P 69125-01-5  
PRO P 78401-94-5

RX(13) OF 66 F ==> P



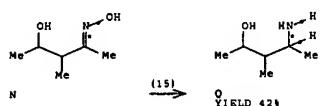
RX(13) RCT F 69125-01-5  
PRO P 78401-94-2

RX(14) OF 66 ...N ==> Q



RX(14) RCT N 78401-96-4  
PRO Q 78420-43-6

RX(15) OF 66 N ==> Q



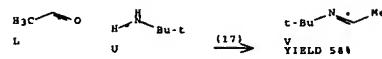
RX(15) RCT N 78401-96-4  
PRO Q 78420-43-6

RX(16) OF 66 R + S ==> T...



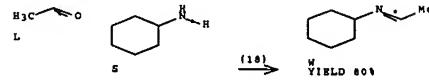
RX(16) RCT R 123-38-6, S 108-91-8  
PRO T 1195-49-9

RX(17) OF 66 L + U ==> V...



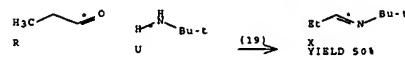
RX(17) RCT L 75-07-0, U 75-64-9  
PRO V 7020-80-6

RX(18) OF 66 L + S ==> W...



RX(18) RCT L 75-07-0, S 108-91-8  
PRO W 1193-93-7

RX(19) OF 66 R + U ==> X...

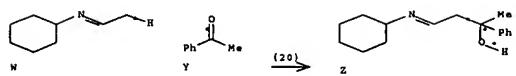


RX(19) RCT R 123-38-6, U 75-64-9  
PRO X 7020-81-7

RX(20) OF 66 ...W + Y ==> Z...

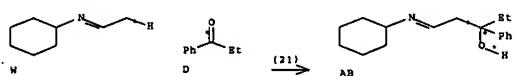
141

142



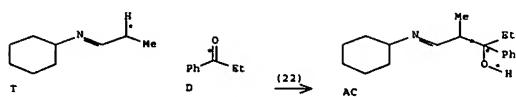
RX(20) RCT W 1193-93-7, Y 98-86-2  
PRO Z 1217-04-5  
CAT 816-43-3 LiNt2

RX(21) OF 66 ...W + D ==> AB...



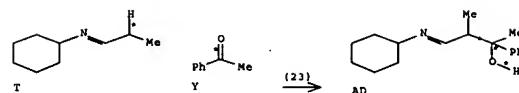
RX(21) RCT W 1193-93-7, D 93-55-0  
PRO AB 343617-82-3  
CAT 816-43-3 LiNt2

RX(22) OF 66 ...T + D ==> AC...



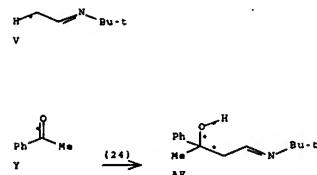
RX(22) RCT T 1195-49-9, D 93-55-0  
PRO AC 343623-11-0  
CAT 816-43-3 LiNt2

RX(23) OF 66 ...T + Y ==> AD...



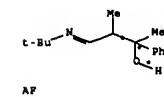
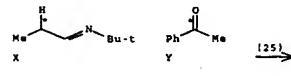
RX(23) RCT T 1195-49-9, Y 98-86-2  
PRO AD 1712-88-5  
CAT 816-43-3 LiNt2

RX(24) OF 66 ...V + Y ==> AB...



RX(24) RCT V 7020-80-6, Y 98-86-2  
PRO AB 343318-81-0  
CAT 816-43-3 LiNt2

RX(25) OF 66 ...X + Y ==> AF...

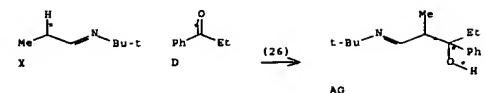


143

144

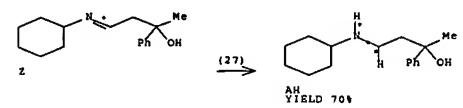
RX(25) RCT X 7020-81-7, Y 98-86-2  
PRO AF 343323-16-0  
CAT 816-43-3 LiN<sub>3</sub>Et<sub>2</sub>

RX(26) OF 66 ...X + D ==> AG...



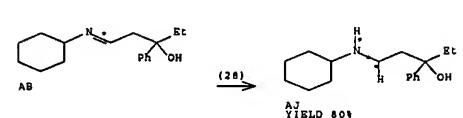
RX(26) RCT X 7020-81-7, D 93-55-0  
PRO AG 343595-95-9  
CAT 816-43-3 LiN<sub>3</sub>Et<sub>2</sub>

RX(27) OF 66 ...Z ==> AH



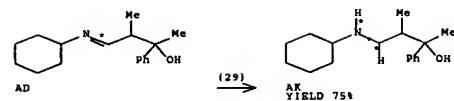
RX(27) RCT Z 1217-04-5  
RGT AI 16853-85-3 LiAlH<sub>4</sub>  
PRO AH 343596-78-1

RX(28) OF 66 ...AB ==> AJ



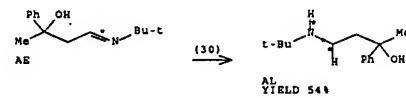
RX(28) RCT AB 343617-82-3  
RGT AI 16853-85-3 LiAlH<sub>4</sub>  
PRO AJ 75243-14-0

RX(29) OF 66 ...AD ==> AK



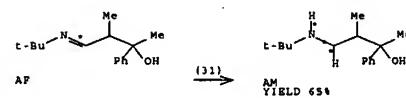
RX(29) RCT AD 1712-88-5  
RGT AI 16853-85-3 LiAlH<sub>4</sub>  
PRO AK 343617-70-9

RX(30) OF 66 ...AE ==> AL



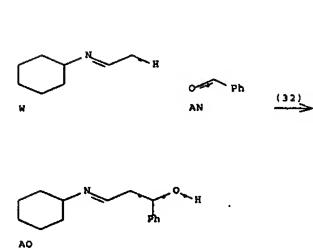
RX(30) RCT AE 343318-81-0  
RGT AI 16853-85-3 LiAlH<sub>4</sub>  
PRO AL 75263-07-9

RX(31) OF 66 ...AF ==> AM



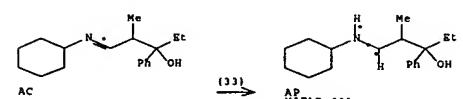
RX(31) RCT AF 343323-16-0  
RGT AI 16853-85-3 LiAlH<sub>4</sub>  
PRO AM 343323-15-9

RX(32) OF 66 ...W + AN ==> AO



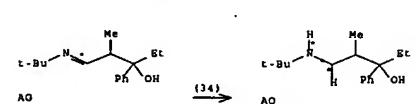
RX(32) RCT W 1193-93-7, AN 100-52-7  
PRO AO 1215-49-2  
CAT 816-43-3 LiN<sub>3</sub>Et<sub>2</sub>

RX(33) OF 66 ...AC ==> AP



RX(33) RCT AC 343623-11-0  
RGT AI 16853-85-3 LiAlH<sub>4</sub>  
PRO AP 343623-09-6

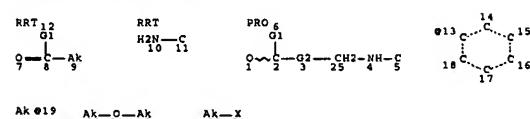
RX(34) OF 66 ...AG ==> AQ



RX(34) RCT AG 343595-95-9  
RGT AI 16853-85-3 LiAlH<sub>4</sub>  
PRO AQ 343595-94-8

## SEARCH HISTORY

>> d stat que 127; d his nofile  
L15 STR



VAR G1=19/20/23/13

REP G2=(0-2) CH2

## NODE ATTRIBUTES:

NSPEC IS RC AT 5  
NSPEC IS RC AT 11  
CONNECT IS EI RC AT 1  
CONNECT IS EI RC AT 9  
CONNECT IS EI RC AT 19  
CONNECT IS EI RC AT 22  
DEFAULT MLEVEL IS ATOM  
GGCAT IS LOC SAT AT 9  
DEFAULT ECLEVEL IS LIMITED

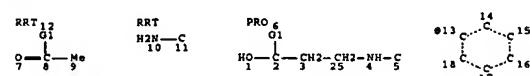
## GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 25

## STEREO ATTRIBUTES: NONE

## \*\*\*\*MAPPINGS\*\*\*\*

NOD SYM ROL NOD SYM ROL  
5 C PRO 11 C RRT  
11 C RRT 5 C PRO  
L19 150 SEA FILE=CASREACT SSS FUL L15 ( 722 REACTIONS)  
L24 STR



VAR G1=19/20/23/13

NODE ATTRIBUTES:

NSPEC IS RC AT 5  
NSPEC IS RC AT 11  
CONNECT IS EI RC AT 19  
CONNECT IS EI RC AT 22  
DEFAULT MLEVEL IS ATOM  
MLEVEL IS CLASS AT 1

DEFAULT ELEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE

\*\*\*\*MAPPINGS\*\*\*

NOD SYM ROL NOD SYM ROL  
5 C PRO 11 C RRT  
11 C RRT 5 C PRO  
L27 8 SEA FILE=CASREACT SUB=L19 SSS FUL L24 ( 26 REACTIONS)100.0% DONE 219 VERIFIED 26 HIT RXNS 8 DOCS  
SEARCH TIME: 00:00.03L18 27925 SEA SSS FUL L15 (367857 REACTIONS) EXTEND  
L19 150 SEA SSS FUL L15 ( 722 REACTIONS)  
SAVE TEMP L19 Y0U362CASRS/A  
L20 STR L15  
L21 3 SEA SUB=L19 SSS SAM L20 ( 7 REACTIONS)  
D SCAN  
D STAT QUB L19  
L22 STR L15  
L23 8 SEA SUB=L19 SSS SAM L22 ( 31 REACTIONS)  
D STAT QUB L21  
L24 STR L20  
L25 1 SEA SUB=L19 SSS SAM L24 ( 1 REACTIONS)  
D SCAN  
L26 66 SEA SUB=L19 SSS FUL L24 ( 219 REACTIONS) EXTEND  
L27 8 SEA SUB=L19 SSS FUL L24 ( 26 REACTIONS)  
SAVE TEMP L27 Y0U362SUB1/A  
L28 0 SEA ABB=ON L27 AND L4

FILE 'CASREACT' ENTERED AT 15:29:11 ON 03 APR 2007

D QUB L4  
D IALL L4 1  
D IALL L4 2  
D STAT QUB L27  
D IALL L27 1-8FILE 'HOMS' ENTERED AT 15:33:48 ON 03 APR 2007  
D STAT QUB L27FILE 'CAPLUS' ENTERED AT 14:58:45 ON 03 APR 2007  
E US2005-520362/APPSL1 1 SEA ABB=ON US2005-520362/AP  
D SCANFILE 'CASREACT' ENTERED AT 14:59:40 ON 03 APR 2007  
E US2005-520362/APPSL2 12 SEA ABB=ON MICHEL D7/AU  
L3 72 SEA ABB=ON 3-AMINO ALCOHOL#L4 2 SEA ABB=ON L2 AND L3  
D SCAN

L5 STR

L6 1 SEA SSS SAM L5 ( 12 REACTIONS)  
D SCAN

FILE 'STNGUIDE' ENTERED AT 15:06:32 ON 03 APR 2007

FILE 'CASREACT' ENTERED AT 15:08:11 ON 03 APR 2007  
SCREEN 1235

L7 1 SEA SSS SAM L5 AND L7 ( 12 REACTIONS)

FILE 'STNGUIDE' ENTERED AT 15:09:47 ON 03 APR 2007

FILE 'CASREACT' ENTERED AT 15:11:33 ON 03 APR 2007

STR L5

L10 1 SEA SSS SAM L9 AND L7 ( 12 REACTIONS)

L11 STR L9

L12 3 SEA SSS SAM L11 AND L7 ( 7 REACTIONS)

D SCAN

D QUB

L13 STR L11

L14 3 SEA SSS SAM L13 ( 7 REACTIONS)

L15 STR L13

L16 4 SEA SSS SAM L15 ( 33 REACTIONS)

L17 3 SEA ABB=ON L16 NOT (L12 OR L14)

D SCAN

D QUB L15